"To Study The Effects & Withdrawal of Atorvastatin, Fenofibrate and Niacin on Lipid and Lipoprotein Profile in Patients of Dyslipidemia"

THESIS

FOR

DOCTOR OF MEDICINE

BUNDELKHAND UNIVERSITY, JHANSI (U.P.)

2005 GAURAV JAIN

Dedicated to My Parents

Department of Medicine,
M.L.B. Medical College
Jhansi (U.P.)

CERTIFICATE

This is to certify that the work entitled ***"To Study The Effects & Withdrawal of Atorvastatin, Fenofibrate and Niacin on Lipid and Lipoprotein Profile in Patients of Dyslipidemia"*** which is being submitted as a thesis for M.D. (Medicine) Examination 2005 of Bundelkhand University, Jhansi, has been carried out by **Dr. Gaurav Jain** in the Department of Medicine, M.L.B. Medical College, Jhansi.

He has put in the necessary stay in the Department as per University regulations, and has fulfilled the conditions required for the submission of thesis according to University regulations.

Dated: 29/10/04

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The method described was undertaken by the candidate himself and the observations recorded have been periodically checked and verified by me from time to time.

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Introduction

Introduction

Atherosclerosis is the leading cause of death and serious morbidity in the present human civilization. It is a progressive disease which begins in childhood and has manifestations in the middle to late adulthood.

Although any artery may be involved the aorta, the coronary and the cerebral systems are the prime targets. Hence myocardial infarction, cerebral infarction and aortic aneurysms are the major consequences of the disease. Moreover, extensive atheromas are friable often yielding of their grumous contents into the distal circulation (atheroemboli) more commonly noted in the kidneys.

Other consequences of acutely or chronically diminished arterial perfusion are gangrene of the legs, mesentric occlusion, chronic ischemic heart disease, ischemic encephelopathy and sudden cardiac death.

Despite a continuing decline in the incidence of atherosclerosis-related death in the past 35 years, deaths from CHD, cerebrovascular disease and peripheral vascular disease accounted for 30% of the 2.3 million deaths in the United states during 1997. Two- thirds of atherosclerosis deaths were due to CHD, about 85% of CHD deaths occurred in individual over 65 yrs.of age. Among the 15% dying prematurely (below age 65), 80% died during their first CHD event. Among those dying of sudden cardiac death in 1997, 50% of the men and 63% of the women had been previously asymptomatic.

These studies illustrate the importance of identifying and management of risk factors for CHD. The major known risk factors are

elevated LDL-C, reduced HDL-C cigarette smoking, hypertension, type II Diabetes mellitus, advancing age and a family history of premature [men 55vr women <65yr] CHD events in a first degree relative, control of the modifiable risk factors is especially important in preventing premature CHD. Observational studies suggest that modifiable risk factors account for 85% of excess risk (risk over and above that of individual with optimal risk factor profiled for premature CHD).

Furthermore these studies indicates that, when total cholesterol levels are below 160 mg/ dl, CHD risk is markedly attenuated, even in the presence of additional risk factor.

This pivotal role of hypercholesterolemia in atherogenesis gave rise to the almost- universally accepted cholesterol-diet-CHD hypothesis.

Relation between an elevated total serum cholesterol (STC) and atherosclerosis (AS) was first noted in 1930's in independant studies by Muller and by Thannhauser and Magendantz. A strong direct co-relation was reported between STC levels and development of IHD in more than 5000 subjects followed for 14 years in Framingham Heart Study (Kannel and co-workers, 1971). Although AS is polygenic in nature and multifactorial in development, the evidence for improvement in coronary disease outcome consequent to lowering low density lipoprotein (LDL) is incontrovertible.

A direct relation exists between LDL levels and development of IHD (Hulley and Rhodes, 1982; Kannel et al, 1984; Ross et al, 1986). In contrast an inverse relationship exists between high density lipoprotein (HDL) levels and development of IHD. (Miller and Miller, 1975; Gordon et al, 1981; Goldbourt et al, 1985).

An understanding of lipoprotein metabolism and how it influences diabetes is of particular importance because of the association of

lipoproteins with CAD, presently the leading cause of death among diabetics. In DM (one of the risk factors for CAD) distrubances of serum lipoprotein concentrations may account for the increased frequency of atherosclerosis in affected patients. (Biermann, 1978; Ganda, 1980).

Increased levels of very low density lipoprotein (VLDL) cholesterol and low density lipoprotein (LDL) cholesterol and a decreased concentration of high density lipoprotein (HDL) cholesterol have been frequently described (Lopes - Virella, 1978; Taylor, 1981; Briones, 1984) in both individuals with non insulin dependant diabetes (NIDDM) and insulin dependant diabetes (IDDM).

Hypertension is quantitatively the largest risk factor for CAD because of early intrinsic vascular abnormalities (probably genetically determined) that are exaggerated by concomitant risk factors and by high blood pressure itself.

New emphasis is now being laid on management of lipid disorders as an area of critical importance in reducing the morbidity and mortality due to coronary events, as evidenced by National Cholesterol Education Programme's (NCEP) aim to target the coronary patients for aggressive lipid lowering therapy. This can be achieved by dietary therapy (as 50% of body cholesterol comes from exogenous sources) or by lipid lowering drugs. The dietary cholesterol can be reduced by reducing oral intake of saturated fats (eg. dairy milk products) and increasing polyunsaturated fat intake.

Statins (Atorvastatin) :

Statins are the HMG-CoA reductive inhibitor which catalyze a early, rate limiting step in cholesterol biosynthesis. [Conversion of HMGCoA To Mevalenate]. By this statins inhibit cholesterogenesis in liver. it also increases the synthesis of LDL receptors, which help in increased removal

of LDL from blood . Statins exert their main effect by reduction of LDL levels although it also reduces the triglyceride level. Some studies show that it helps in increasing HDL levels.

Along with its lipid lowering property statins also stabilizes the plaque and reduces the thromboembolic phenomenon.

Nicotinic Acid (Niacin) :

One of the oldest drug used to treat dyslipidemia and is most versatile in that it favorably affects virtually all lipid parameters. Niacin is the best available agent for increasing HDL-C [30%-40%] it also lowers triglycerides by 35%- 45% and reduces LDL-C levels by 20% -30%,only lipid lowering drug that reduces LP(a) level significantly (40%).

F1bric Acid Derivatives (Fenofibrate) :

Mechanism by which fibrates lower lipoproteins levels or raise HDL levels remain unclear, recent studies suggest by interacting with peroxisome proliferator activated receptors (PPAR) they increase LPL synthesis and enhance the clearance of triglycerides-rich lipoproteins, Fibrate mediated increase in HDL-C are due to PPARα stimulation of apoA-I and apo A-II expression, which increase HDL levels.

Most of the fibric acid agents have potential antiatherothrombotic effects including inhibition of coagulation and enhancement of fibrinolysis. These salutary effects also could alter cardiovascular outcomes by mechanisms unrelated to any hypolipidomic activity.

Fibrates usually are the drug of choice for treating severe hypertriglyceridemias (decrease up to 50%), also increase HDL-C, LDL-C levels may be unchanged or increase.

Review of Literature

Atherosclerosis and its clinical sequelae coronary artery disease (CAD) is the leading cause of death in most industrialized countries, and its importance as a major public health problem is increasing in developing countries. The initial connection between cholesterol and atherosclerotic plaques began in 1912 when Anitschkow reported finding atherosclerotic plaques similar to those occuring in humans, in rabbits fed with diets high in cholesterol.

Atherosclerosis in coronary arteries is nearly always seen in epicardial (extramural) portion of vessels, while the intramural coronary arteries are spared. The highest incidence is at a short distance from the ostia. Main stem of four major coronary arteries are involved. Right, Left main, Left Anterior descending and Left circumflex. The atherosclerotic plaque is composed of fibrous tissue (80%), extracellular lipid (5%), calcium (5%), macrophages and other cells 10%). The fibrous tissue increases as the plaque size increases.

Risk Factors For Atherosclerosis :

1. Male gender
2. Family history of premature IHD.
3. Hyperlipidemia.
4. Cigarette smoking
5. Hypertension.
6. Low HDL cholesterol
7. Diabetes mellitus
8. Hyperinsulinemia.

9. Abdominal obesity

10. High lipoprotien a levels.

11. Personal history of cerebrovascular disease (CVD) or peripheral vascular disease (PVD).

Risk factor concept implies that a person with either one or more risk factors is more likely to develop a clinical atherosclerotic event than a person with no risk factors. The most potent risk factors out of the above listed are hyperlipidemia, hypertension and cigarette smoking.

Endothelial Function And Lipid Metabolism In Arterial Wall

Normal arterial wall consists of 3 layers; intimia, media and adventitia. Intact endothelium regulates vascular tone by elaborating endothelium derived relaxing factor (EDRF) EDRF is actually nitric oxide (NO) or NO containing donor that mediates its vasodilator effects by activating guanylate cyclase (through c-AMP) EDRF inhibits monocyte adhesion, inhibits vascular smooth muscle contraction (VSMC) by EDRF and also inhibits abnormal growth of VSMC. It also inhibits platelet aggregation and adhesion (by prostacyclin PGI_2 and EDRF). Endothelial dysfunction could thus result in initiation of atherosclerosis.

Arterial wall cells can synthesize fatty acids, triglycerides, phospholipids and cholesterol from endogenous substrates for its repair and regeneration of membrane, but VSMC preferentially utilize lipids from plasma lipoproteins that are transported through endothelial cells in pinocytic vesicles.

VSMC possess specific receptors on the surface for some apoproteins present on the surface of these lipoproteins. Thus pinocytic vesicles (containing lipoproteins) gain entry inside SMC and fuse with lysosomes, where lysosomal enzymes cause breakdown of protein part

from lipoprotein and cholesterol ester get liberated which later gets converted into free cholesterol inside VSMC.

Hyperlipidemia And Atherosclerosis:

Several factors have been considered to predispose to atherosclerosis, but of these only elevated LDL cholesterol concentration and low levels of HDL cholesterol are the direct risk factors. All the other risk factors cited above worsen the atherosclerotic process but in the absence of direct risk factors they do not cause atherosclerosis.

A. Serum Total Cholesterol (STC)

Cann et al, (1977) reported higher levels of STC in proven CAD cases than those without CAD. Kannel et al, (1977) found that the incidence of CAD at STC levels of 220 mg/dl was nearly two fold than at levels of 180mg/dl. Kannel and co-workers also established the role of hypercholesterolemia in causing CAD in the Framingham heart study (1971). Studies at Oslo (West Lund, 1964; Nicolasayen, 1966) have elaborated the role of lipids in atherosclerosis. Martin and colleagues reported on unequivocal relationship between baseline total serum cholesterol (STC) and mortality from cardiovascular disease in Multiple Risk Factor Intervention Trial (MRFIT). They reported 3 fold increase in risk of CAD at STC levels above 240 mg/dl than at levels less than 200 mg/dl.

Garret et al, (1964) attempted to relate the extent of vascular damage to STC. High cholesterol levels were reported in cases of sudden death due to myocardial infarction by Chajman and Marney, (1964).

Henry Scott et al, (1982) did quantitative analysis of epicardial coronary artery and showed relation of STC and STG levels to the amount and extent of coronay artery narrowing by atherosclerotic plaque in coronary heart disease. He showed that the subjects with normal STC and

STG levels (group I) had significantly fewer major coronary arteries severely narrowed by atherosclerotic plaque than did the subjects with hypercholesterolemia (group II) or hypertriglyceridemia (group III) or both (group IV).

Increase in both degree and duration of lipemia in patients with evidence of CAD has been reported by many workers. (Waldow et al, 1954, Barritt, 1956; Bronte Stewart and Blackburn, 1958; Bouchier and Bronte Stewart, 1961).

At young age (35-50 years) myocardial infaction is associated with higher triglyceride levels while in higher age group (> 50 years) plasma total cholesterol levels are more than plasma triglyceride levels. (Carlson, 1960).

B. Serum Total Triglycerides (STG)

Several studies have shown that an elevation of STG is common in patients with CAD (Albrink et al, 1959; Hulley et al, 1980) Carlson and Bottiger, (1972) reported that incidence of CAD rose linearly with increasing plasma triglycerides. However, there is a great debate as to whether VLDL is the directly operating factor in producing CAD or is it the association of increased LDL and decreased HDL levels which is causative (Bilheimer, 1972).

C. Low Density Lipoprotein (LDL) Cholesterol

Concentration of LDL cholesterol is directly related to and is predictive of the risk for CAD. (Gordon et al, 1981; Hulley and Rhodes, 1982; Kannel et al, 1984). Mortality rate due to CAD in different communities are directly and linearly related to STC and LDL cholesterol levels (Lewis et al, 1978).

Increase in STC levels is associated with an increase in LDL levels. LDL exists in three forms - small LDL, dense LDL and LDL pattern B. It is now known that dense LDL fraction is more atherogenic.

Levgiyama et al demonstrated that native LDL had no inhibitory effect on endothelium whereas oxidized LDL totally abolished endothelial dependant vasorelaxation. Peroxidation of polyunsaturated fatty acids in LDL occurs in VSMC and endothelial cells (EC) of the vessel wall. This LDL is chemoattractant to monocytes and facilitates the recruitment of circulating monocytes. It also increases production of growth factors and cytokines by macrophages and endothelial cells. The degradation of endothelial nitric oxide (NO)by oxidized LDL leads to decreased vasodilation and increased vasoconstriction in coronary arteries. LDL is also cytotoxic in its own right.

Plaque morphology rather than its size determines the development of acute coronary episode. Plaques rich in lipid, having high macrophage density and thin fibrous cap are more prone to rupture, resulting in formation of occlusive thombus. Such plaques are known as unstable plaques. Coree and colleagues reported that increase in the lipid pool of plaque increases its chances of rupture. The oxidized LDL probably acts by its cytotoxic effect on endothelial smooth muscle or other cells and also stimulates macrophages to secrete a metalloproteinase that digests the connective tissue matrix of the plaques' fibruous cap, thus weakening it to hemodynamic stress.

D. High Density Lipoprotein (HDL) Cholesterol

HDL Cholesterol concentrations are even more strongly predictive of the risk for CAD in most studies. (Miller and Miller, 1975; Goldbourt and Medalis, 1979; Gordon et al, 1981). The ability of HDL cholesterol to

predict development of coronary atherosclerosis is eight times more than that of STC (Gordon et al, 1977).

HDL carries 20% of STC. Subclasses of HDL can be fractioned by zonal ultracentrifugation, most abundant of which are HDL and HDL_2 Out of these HDL_2 appears to have stronger inverse relationship with occurrence of CAD and accounts for different levels of HDL cholesterol between men and women (Gofman et al, 1954). It is reasonable to view low HDL as an additive atherosclerotic risk factor if LDL is elevated but not when LDL level is low. Framingham Study showed that low HDL level was a more potent risk factor for CAD than either STC or LDL.

Possible mechanisms of antiatherogenic effect of HDL :

(i) Reversal of cholesterol transport from the peripheral cells to liver for removal from the body. (Miller and Miller, 1975).

(ii) Inhibition of LDL uptake by cells at the LDL receptor site.

(iii) Cholesterol efflux : HDL stimulates endothelial repair and PGI-2 synthesis by endothelial cells. PGI-2 in turn hydrolyze cholesterol esters in SMC thus forming free cholesterol. This can be easily removed from cells in arterial wall.

(iv) Inhibition of vascular smooth muscle cells.

(v) Facilitates metabolism of very low density lipoprotiens (VLDL) and intermediate density lipoprotiens (IDL).

<u>Factors modulating plasma lipids and lipoproteins in humans</u> :

A. *Age and Sex :*

Significant relationship between sex and age of a person and his plasma lipid levels has been seen. Some workers have reported that the mean level among females never exceed 85 mg% while in men the mean

level reaches its maximum in age group 40-59 years and is about 107 mg% (Schaefer and Mechemias, 1965). In another study females were found to have a markedly lower level (mean value 130 mg/dl) than males (mean value 185 mg/dl).

In most populations, women have been shown to have a higher level of HDL than men at all ages following puberty. A drop in HDL levels seen in males at around the time of puberty has been related to the degree of sexual maturation (Frenichs et al, 1978; Morrison et al, 1979) Transient rise in HDL_2 is also reported at or near the time of ovulation (Bareley et al, 1965).

HDL levels also change with age. In males, levels are stable till puberty, show a decline during adolescence, relatively stable levels in adulthood then plateau in old age. Females show a small linear increase in HDL from childhood to about 60 years after which no effect of age is apparent. (Heise et al, 1980).

An age dependant increase of triglyceride levels during 3^{rd} and 4^{th} decades of life have been reported in a study of 500 swiss males (Hyden, 1967; Dyerberg and Hijerne, 1972).

B. Weight:

Albrink et al, (1962) assumed that the rise in triglycerides and cholesterol levels with age might be due to age related weight gain. Increasing hypertriglyceridemia in weight gainers has been reproted (Hyden, 1969).

C. Diurnal and Seasonal Variation ;

Cholesterol and phospholipids show a minimal diurnal variation. A seasonal variation is often seen in triglyceride levels with the value being higher in winters than in summers (Carlson and Lindstadt, 1968).

D. Obesity :

HDL levels are lower in obese individuals as compared to non obese (Wilson et al, 1972; Carlson et al, 1975). In some studies increase in HDL levels along with fall in VLDL and TG concentrations have been reported during the course of weight loss (Wilson et al, 1972).

E. Physical Activity :

Accelerated rate of chylomicron removal after exercise and its accentuation after habituation to exercise has been observed (Kmt et al, 1963). Definite fall in TG levels after exercise has been reported by many workers. (Kenttinan, 1963; Hellesey et al, 1964). High levels of HDL are reported with high level of endurance type exercise like long distance running, tennis and soccer . (Weed et al, 1977; Lehtonen et al, 1978; Vedak et al, 1980), whereas a drop in HDL was observed with calorie restriction in the absence of exercise (Weltman et al, 1980).

According to the National Cholesterol Education Programme (NCEP) expert panel on detection, evaluation and treatment of high Blood Cholesterol in adults (Adults treatment Panel III), major risk factors (exclusive of LDL cholesterol) for CHD are as follows :

- Cigarette smoking
- Hypertension (blood pressure $\geq$ 140/90mm of Hg or on antihypertensive medication).
- Family history of premature CHD (CHD in male first degree relative <55yrs; CHD in female first degree relative <65 years).
- Age (men $\geq$ 45 years; women $\geq$ 55 years).

Diabetes is regarded as a coronary heart disease risk equivalent i.e. a condition that carries an absolute risk for developing new CHD equal to the risk for having recurrent CHD events in persons with established CHD.

Hence forth, hypercholesterolemia and hypertriglyceridemia are considered as directly and indirectly predisposing factors for ischemic heart disease and it is presumed that lipid lowering drugs may be beneficial in the primary and secondary prevention.

Statins

The statins are the most effective and best-tolerated agents for treating dyslipidemia. These drugs are competitive inhibitors of 3-hydroxy-3methylglutaryl coenzyme A (HMG)-CoA) reductase, which catalyzes an early, rate-limiting step in cholesterol biosynthesis. Higher doses of the more potent statins (e.g., atorvastatin and simvastatin) also can reduce triglyceride levels caused by elevated VLDL levels. Some statins also are indicated for raising HDL-C levels, although the clinical significance of these effects on HDL-C remains to be proven.

Five large, well-controlled clinical trials have documented the efficacy and safety of simvastatin, pravastatin, and lovastatin in reducing fatal and nonfatal CHD events, strokes, and total mortality.

Mechanism of Actions :

Statins exert their major effect – reduction of LDL levels – through a mevalonic acid like moity that competitively inhibits HMG-CoA reductase by product inhibition (Alberts et al., 1980).

Statins affect blood cholesterol levels by inhibiting cholesterol-genesis in the liver, which results in increased expression of the LDL receptor gene, which increases the synthesis of LDL receptors (Brown and Goldstein,

1998) ? Degradation of LDL receptors also is reduced (Brown et al., 1978). The greater number of LDL receptors on the surface of hepatocytes results in increased removal of LDL from the blood (Bilheimer et al., 1983), there by lowering LDL-C levels.

Some studies suggest that statins also can reduce LDL levels by enhancing the removal of LDL precursors (VLDL and IDL) and by decreasing hepatic VLDL production.

Triglyceride levels greater than 250mg/dl are reduced substantially by statins and the percent reduction achieved is similar to the percent reduction in LDL-C. If baseline triglyceride levels are below 250mg/dl reduction in triglycerides do not exceed 25 percent irrespective of the dose of statin used.

Pontrelli L Parris W. Adelik, Cheung RC et al investigated the potential hypolipidemic effects of atorvastatin, a 3- hydroxy, 3- methyl glutaryl coenzyme A reductuse inhibiter with good triglyceride lowering properties, in patients with combined dyslipidemia and evidence of impaired fasting glucose or type II diabetes 20 patients were recruited for the study and two subgroups were made, one group receiving atorvastatin (80mg/day) with other placebo for 60 days. At the end of study treatment with atorvastatin resulted in a statistically significant reduction in total cholesterol (41%) LDL cholesterol (55%). triglycerides (32%)and apoB (40%). Mean LDL particle diameter significantly increased 25.29± 0.24nm to 26.51.

Results suggested that atorvastatin beneficially alters the atherogenic lipid profile in these patients.

Atalar E . Ozmen F. Hazenedraoglu I. Ault Ozer N. Ovuric K. Akroyek S. Kes S. et al studied the effect of short term atorvastatin

treatment on the fibrinolytic system and systemic inflammatory status and on apoptosis in hyperlipidemic patients with coronary artery disease. Study population consisted of 36 hyperlipidemic patient with stable CAD, untreated with lipid lowering medications, they received 10 mg/day atorvastatin for 12 weeks. After treatment LDL decreases by 39%, total cholesterol decreases by 32% and triglycerides decreased by 22% and HDL-C increased by 13%. These effects were associated with a decrease in plasma fibrinogen from 331-298 mg/dl and SL selection levels from 666 ± 201-584 ± 62 ng/ml. and s Fas level & GFC increased from 3754-4873 pg/ml and from 3.5-5.6 us/ ml respectively. There results suggest that lipid lowering with atorvastatin therapy significantly increases GFC, decrease fibrinogen levels and cause leukocyte deactivation.

Parhofer KG laubach E, Bamett PH studied the effect of atorvastatin on postprandial lipoprotein metabolism in hypertriglyceridemic patients and found that atorvastatin improves postprandial lipoprotein metabolism in addition to decreasing fasting lipid levels in hypertriglyceridemia .

Spostto AC, Santos RD, Amaricso RF, Ramires JA, John chapman M, Maramhoo RC, studied the effect of atorvastatin (10mg) at low dose and high dose (40mg) upon the intravascular metabolism and plasma kinetics of chylomicron like emulsions in 45 hyperlipidemis subjects for 6 wks, and found that atorvastatin treatment accelerates the plasma clearance of chylomicron like emulsions and reduce recirculation of fatty acids in subject with atherogenic hyperlipidemia.

Hepatic lipase activity is significantly higher in population compared with an age matched control group without diabetes. Hepatic lipase is involved in the metabolism of several lipoprotein and may contribute to the atherogenic lipid profile in type 2 diabetes . Berk-Planken H , Hoogerbrugge N, Stolk RP, Bootsma AH, Jarsen H et al studied the

atorvastatin 10mg and atorvastatin 80mg an Hepatic lipase activity in 198 patients with type 2 diabetes for 30 wks. [Diabetes Atorvastatin Lipid Intervention study] and found that Atorvastatin treatment in diabetic dyslipidemia results in a significant dose dependent decrease in Hepatic lipase activity.

The GREEK Atorvastatin and Coronery heart disease Evaluation (GREACE) study compared two standards of lipid lowering treatment in 1000 patients with coronary heart disease. Structured care aimed at achieving the low density lipoprotein cholesterol (100mg/ld), goal described in the NCEP ATP II & III guidelines for patients with CHD. Structured care was associated with a significant reduction in overall mortality and coronary events compared to usual care

Schaefer EJ. Mc Namara JR. Tayler T. Daly JA. Gleason JA. Seman LJ. Ferrari A. Rubenstein JJ studied the effects of atorvastatin on fasting and postprandial lipoprotein subclasses in coronary heart disease patients versus control subjects in 2002 Oct. The effects of atorvastatin at 20, 40, and 80 mg/day on plasma lipoprotein subclasses were examined in a randomized, placebo-controlled fashion over 24 weeks in 103 patients in the fasting state who had coronary heart disease (CHD) with low-density lipoprotein (LDL) cholesterol levels →130 mg/dl. The effects of placebo and atorvastatin 40 mg/day were examined in 88 subjects with CHD in the fasting state and 4 hours after a meal rich in saturated fat and cholesterol. These findings were compared with results in 88 age- and gender-matched control subjects. Treatment at the 20, 40, and 80 mg/day dose levels resulted in LDL cholesterol reductions of 38%, 46%, and 52% [all p ← 0.0001), triglyceride reductions of 22%, 26%, and 30% (all p ← 0.0001), and high-density lipoprotein [HDL cholesterol increases of 6%, 5%, and 3%, respectively (all p ← 0.05 at the 20- and 40-mg doses]. The lowest total cholesterol/HDL cholesterol ratio was observed with the 80 mg/day

dose of atorvastatin (p ← 0,0001 vs placebo). Remnant-like particle (RLP) cholesterol decreased 33%, 34%, and 32%, respectively (all p ← 0.0001). Lipoprotein(a) [Lp(a)] cholesterol decreased 9%, 16%, and 21% (all p ← 0.0001], although Lp(a) mass increased 9%, 8%, and 10%, respectively (all p ← 0.01). In the fed state, atorvastatin 40 mg/day normalized direct LDL cholesterol (29% below controls), triglycerides (8% above controls), and RLP cholesterol (10% below controls), with similar reductions in the fasting state. At this same dose level, atorvastatin treatment resulted in 39%, 35%, and 59% decreases in fasting triglyceride in large, medium, and small very LDLs, as well as 45%, 33%, and 47% reductions in cholesterol in large, medium, and small LDL, respectively, as assessed by nuclear magnetic resonance [all significant, p ← 0.05), normalizing these particles versus controls (77 cases vs 77 controls).

Stern RH. Yang BB. Hounslow NJ. MacMahon M. AbelRB. Olson SC studied the pharmacodynamics and pharmacokinetic-pharmacodynamic relationships of atorvastatin, an HMG – CoA reductase inhibitor and found that following initiation of dosing, statistically significant decreases in total cholesterol. LDL-cholesterol and LDL-apolipoprotein B were observed within 24 hours and in LDL-C within 72 hours. Following discontinuation of drug dosing, statistically significant increases were observed in total cholesteroland LDL-cholesterol within 48 hours and in LDL-cholesterol and LDL apolipoprotein B within 72 hours. In conclusion, atorvastatin produces marked LDL - cholesterol reductions the mean dose-response relationship is log linear, almost all individual dose-response curves parallel the mean dose response curve onset and cessation of action are rapid, the estimated and measured LDL – cholesterol are the same, LDL-cholesterol and LDL-Apo B reductions are similar, and plasma concentrations are not correlated with LDL-cholesterol reduction at a given dose.

Statins and Endothelial Function :

Statin therapy improves coronary vasodilation in response to acetylcholine. Statins stabilize endothelial cell nitric oxide synthase mRNA, thereby enhancing synthesis of endothelial cell nitric oxide (Laufs et al., 1998) . Statin therapy reverses endothelial dysfunction as monitored by vasoactivity within a short period of one month.

Statins and Plaque Stability :

As discussed earlier, the vulnerability of plaques to rupture and thrombosis is of greater clinical relevance than the degree of stenosis they cause (Gutstein and Fuster, 1999). Statins may affect plaque stability in a variety of ways. There are reports that statins inhibit monocyte infiltration into the artery wall in a rabbit model (Bustos et al., 1998) and inhibit macrophage secretion of matrix metalloproteinases in vitro (Bellosta et al., 1998). The metalloproteinases degrade all extracellular matrix components and thus weaken the fibrous cap of atherosclerotic plaques.

Statins and Inflammation :

Appreciation of the importance of inflammatory processes in atherogenesis is growing (Ross, 1999), and statins have been suggested to have an antiinflammatory role. So they are helpful in prevention of atherosclerosis.

Statins and Coagulation :

Statins reduce platelet aggregation (Hussein et al., 1997a), and in vitro model systems indicate that statins reduce the deposition of platelet thrombi on porcine aorta.

Nicotinic Acid (Niacin) :

Nicotinic acid (niacin, pyridine-3-carboxylic acid) is one of the oldest drugs used to treat dyslipidemia and is the most versatile in that it

favorably affects virtually all lipid parameters. Niacin is a water-soluble B-complex vitamin that functions as a vitamin only after its conversion to nicotinamide adenine dinucleotic.

The hypolipidemic effects of niacin require larger doses than are required for its vitamin effects. Niacin is the best agent available for increasing HDL-C (increments of 30% to 40%); it also lowers triglycerides by 35% to 45% (as effectively as fibrates and the more potent statins) and reduces LDL-C levels by 20% to 30%. Niacin also is the only lipid – lowering drug that reduces Lp (a) levels significantly, by about 40%.

Mechanism of Action **:**

In adipose tissue, niacin inhibits the lipolysis of triglycerides by hormone-sensitive lipase, which reduces transport of free fatty acids to the liver and decreases hepatic triglyceride synthesis. In the river niacin reduces triglyceride synthesis by inhibiting both the synthesis and esterfication of fatty acids.

Niacin raises HDL-C levels by decreasing the fractional clearance of apoA-I in HDL rather than by enhancing HDL synthesis.

Elam MB humringhake DB Davis KB, Garg R, Johnson C, Egan D,\ Kostis JB. Shefis DS, Brinton EA, et al studied the effect of niacin on lipid and lipoprotein levels and glycemic control in patients with diabetes and peripheral arterial disease. Study was conducted on 468 patients out of which 125 are of diabetes with peripheral arterial disease, patients received 3000 mg/day or maximum tolerated dosage of niacin for 60 wks. [12 with active run- in and 48 wk double blind]. After treatment niacin significantly increased HDL-C by 29% and 29% and decreased tridycerides by 23% and 28% and low density lipoprotein cholesterol by 8% and 9% respectively in patients with and without Diabetes. Levels of HbAIC were unchanged from baseline to follow up in participants with diabetes treated with niacin.

Study suggests that lipid modifying dosage of niacin can be safely used in patients with diabetes and that niacin therapy may be considered as an alternative to statin drugs or fibrates for patients with diabetes in whom these agents are not tolerated or fail to sufficiently correct hyportriglyceridemia or low HDL-C levels.

Grundy SM, vegaGL, Me gavern MC, Tulloch BP Kendall DM, Fitz Patrick D, Ganda OP et al studied the efficacy, safety and tolerability of once-daily niacin for the treatment of dyslipidemia associated with type 2 diabetes. Diabetic dyslipidemia is characterized by high triglyceride level, low high density lipoprotein cholesterol, small dense low density lipoprotein particle, with high free faitty acids. Study was done on 148 patients 49 were taking placebo. 45 were taking 1000 mg ER Niacin for 16 weeks. After 16 weeks. Treatment, dose dependent increase in HDL cholesterol level [± 19% & ± 24] and reduction in triglyceride levels (-13% & -28%) were observed. Baseline & 16 wk glycosylated Hb levels were 7.13% & 7.11% respectively in the placebo group, 7.28% & 7.3% respectively in 1000 mg ER Niacin group and 7.2% and 7.5% respectively in the 1500mg ER niacin group. The study shows that low doses of ER Niacin (1000 or 1500 mg/dl) are a treatment option for dyslipidemas in patients with type 2 diabetes.

High dose of niacin has been shown to impair glucose control in patients with non insulin dependent Diabetes mellitus. Rindos JR. Achacosa S, et al undertook a study to determine, if low dose niacin has a similar effect in patients receiving niacin 500mg three times daily for 2 month with fasting bid. Sugar was measured after every 2 weeks and hemoglobin A (Ic) and lipid profile determined after 8 week, statistical analysis was performed using a t-test for related groups. Mean fasting blood sugar was statically higher during niacin therapy versus baseline (131 mg/dl $\pm$ 27 vs 161mg/dl ± 40), no change was noted in HbAlC, there

was a trend in a decrease in total cholesterol, LDL - and triglyceride. HDL was statistically higher after niacin therapy.

Pair J, Lin M, Kesala RL, Von J, charles MA et al tested the hypotheses that niacin is effective for the separate treatment of abnormalities of LDL particle size, HDL2 percentage and LP(a) without potential negative effect on glycosylated Hb, and found that after niacin therapy LDL particle size increases, small dense LDL particle mass decreases, total HDL-C mass increased and LP(a) decreases. Mean HbAIC levels was improved during treatment using increased oral agents and insulin treatment doses in more that 90% of the patients.

Fibric Acid Derivaties -Fenofibrate :

Mechanism of Action

Despite extensive studies in human beings, the mechanisms by which fibrates lower lipoprotine or raise HDL levels, remain unclear. recent studies suggest that many of the effects of these compounds on blood lipids are mediated by their interaction with peroxisome proliferator-activated receptors (PPARs). Fibrates reduce tirglycerides through PPARα-mediated stimulation of fatty acid oxidation, increased LPL synthesis, and reduced expression of apoC-III. Fibrate-mediated increases in HDL are due to PPARα stimulation of apoA-I and apoA-II expression (Staels and Auwerx, 1998), which increases HDL levels. Most of the fibric acid agents have potential antiatherothrom botic effects, including inhabitation of coagulation and enhancement of fibrinolysis. These salutary effects also could after cardiovascular outcomes by mechanisms unrelated to any hypolipidemic activity.

Sasaki J. Yamamoto K. Ageta M studied effects of tenofibrate on high density lipoprotein particle size in patients with hyperlipidemia, in it fifty hyperlipidemic patients [31 men, 19 women; mean (SD)) age, 54.6

(12.7) years] were enrolled. Serum total cholesterol and triglyceride levels were significantly reduced with fenofibrate treatment compared with placebo [9.4% (P = 0.007) and 34.4% (P 0.001)], respectively], whereas HDL-C levels were significantly elevated [by 25.8% (P – 0.001)]. Lipoprotein lipase [LPL] activity, LPL protein level, and hepatic triglyceride lipase activity increased by 10.5%, 13.4%, and 11.4%, respectively. The amount of HDL3 increased significantly with fenofibrate compared with placebo [P – 0.001]. Fenofibrate was well tolerated during the study. These findings indicate that fenofibrate therapy increased the HDL subfraction with the smallest diameter [HDL3], which is largely responsible for withdrawing cholesterol from peripheral cells.

Fenofibrate has consistently been shown to increase HDL, with relative change, ranging from 15% to 30%. When baseline HDL is < 35 mg/dl the increase is much more pronounced and may even reach 40% to 50% . In two trials conducted in clinical practice settings in Belgium (6months n=1545) and Germany (3 months n=9884) treatment with fenofibrate resulted in significant increase in HDL of 19% and 23% respectively. The increase in HDL were baseline dependent and were most marked when baseline HDL was < 35 mg/dl where mean increase reached 41% and 44% respectively In both trials, a high percentage of patients reached post treatment levels that were > 45 mg/dl .

In the German trial. The over all increase in mean HDL were observed across a variety of subgroups. In the Belgium trial 735 patients took part in a 6 month extension phase. During this extension phase, the increases in HDL observed on fenofibrate treatment in the first 6 month period were maintained over the 12 month period.

A high density lipoprotein cholesterol level < lmmol/I is associated with increased cardiovascular morbidity and mortality. Ic Raux CW,

Marphy E, Seed M, studied the fenofibrate 267 mg/d and found that fenofibrate 267 mg/d is well tolerated and can achieve significant increase in HDL-C levels in clinical practice.

Micronised fenofibrate is indicated for the treatment of dyslipidemia. Recently a new tablet formulation of micronised fenofibrate has become available with greater bioavailability than the older capsule formulation. The micronised fenofibrate 160mg tablet is bioequivalent to 200mg capsule. Microised fenofibrate 200mg capsule once daily produced greater improvement in TG, and generally in HDL levels than HMG-CoA inhibitor simvastatin (10 or 20mg/day) parvastatin 20mg/day or atorvastatin 10-40mg/ld. Micronised fenofibrate 200mg once daily was associated with significantly greater improvements from baseline in TC.LDL-C, HDL-C, and TG levels than placebo in patients with type 2 diabetes mellitus enrolled in the double blind randomised Diabetes atherosclerosis intervention study [DAIS] Morever angiography showed micronised fenofibrate was associated with significantly less progression of coronary atherosclerosis than placebo.

Aims and Objectives

Aims And Objectives

1. To find out the patients of deranged lipid profile who need drug management by their lipid profile examination.

2. To study the effects of Atorvastatin, Niacin and Fenofibrate on their lipid profile after 1 and 3 months of treatment.

3. To study the effects of withdrawal of Atorvastatin, Niacin and Fenofibrate on their lipid profile after 1 and 3 months of treatment.

Material and Methods

Material And Methods

Subject were chosen from patients coming in OPD & wards of M.L.B. Medical College and hospitals

Subjects were chosen for drug therapy on the basis of guidelines of NCEP. ATP III. According to which lipids levels are classified as below.

Total Cholesterol :

< 200mg/dl	Desirable
200-239mg/dl	Borderline high
≥ 240 mg/dl	High

HDL – Cholesterol :

<40mg/dl	Low (consider <50mg/dl as low for women)
>60mg/dl	High

LDL – Cholesterol :

< 100 mg/dl	Optimal
100-129 mg/dl	Near optimal
130-159 mg/dl	Borderline high
160-189 mg/dl	High
≥190 mg /dl	Very high

Triglycerides :

< 150 mg/dl	Normal
150-199 mg/dl	Borderline high
200-499 mg/dl	High
≥ 500	Very high

According to NCEP ATP-III guidelines LDL-C goal levels depend upon the presence of Risk factor for coronary Heart disease. These risk factors are.

- Cigarette smoking
- Hypertension (B.P.>140/90 mm Hg or on antihypertensive treatment)
- Low HDL cholesterol (< 40 mg/dl)
- Family history of premature CHD [CHD in males first degree relatives <55yr. CHD in female first degree relative < 65yr.]
- Age (men ≥ 45 yr. women ≥ 55 yr.)

Based on these risk factors LDL goal & LDL levels at which drug therapy for LDL should start as follows.

Risk Category	LDL Goal mg %	LDL level at which Drug therapy should start mg %
1. CHD or CHD risk equivalents (10yr. risk > 20%)	< 100	≥ 130
2. 2 + Risk factor with 10 yr. risk 10%-20%.	< 130	≥ 130
3. 2 + Risk factor with 10 yr. risk 10%.	< 130	≥ 160
4. 0-1 Risk factor.	< 160	≥ 190

CHD risk equivalents companies of

- Clinical forms of atherosclerotic – diseases
  - Peripheral arterial disease
  - Abdominal aortic aneurysm
  - Symptomatic carotid artery disease
- Diabetes
- Multiple risk factors that confers a 10yr. risk for CHD>20%.

If the patient have TG level > 150 mg% but less then 500 than primary aim of therapy is to achieve the target goal for LDL.

If TG is > 500mg % initial aim is to prevent acute pancreatitis through TG lowering.

ATP III does not specify a goal for HDL raising. In all persons with low HDL-C cholesterol the primary aim of therapy is LDL cholesterol. According to these patients are divided in to 3 groups

Group - I : patients having ↑ LDL according to their risk category & TG < 500mg% receiving atorvastatin 20mg/day.

Group - II : patients having predominantly ↑ TG (≥250mg%) receiving fenofibrate 160mg tab/day.

Group - III : patients having predominantly ↑ HDL (≤ 35mg%) or having total cholesterol/HDL ratio > 4.5. receiving niacin 325mg. BD initially and then niacin 500mg BD.

METHOD

Subject were allowed to eat their usual diet and to lead their routine life. Subjects were advised to either reduce or to stop smoking. Similarly they were advised to either reduce or not to use alcohol during this period. Drug compliance were assured by asking them on every visit about their drug intake.

Detailed history regarding the diseases and drug intake was taken which is followed by physical examination and routine investigation.

Design of Test **:**

All the selected subjects of each groups were asked to have dinner on the previous evening and after an overnight fast of 12 hrs, fasting blood

samples were collected and were instructed not to take anything except water during that period.

Five fasting samples of blood were collected from each subject for lipid and lipoprotein analysis throughout the study.

One each at registration (Basal), any day during 4th week and 12th week while using atorvastatin, fenofibrate & niacin in respective group.

Two samples out of five, were taken at 1st and 3rd month of the withdrawal of atorvastatin, fenofibrate & niacin in respective group.

Serum was separated from blood within half an hour by centrifuging, and with the supernatant of the samples the following tests were done.

1. Serum total cholesterol (STC) estimation was done by enzymatic procedure of Allain and Koeschlau using cholesterol esterase, cholesterol oxidase and peroxidase in a single reagent.

   Estimation was done by one step method utilizing the kit provided by "Monozyme India Limited'.

Procedure **:**

Three test tubes were taken and labelled as test (Tc), standard (s) and Blank (b) and then following steps were undertaken.

	Test (Tc)	Standard (s)	Blank (b)
Enzyme reagent (1)	1.0ml	1.0ml	1.0ml
Cholesterol standard (3) (200mg%)		0.01ml (10µl)	
Serum	(0.01ml) (10µl)		
Distilled water	0.1 ml	0.1 ml	0.1 ml

Contents of all the tubes were mixed well and then incubated at room temperature for 10 minutes.

Optical density (O.D.) of each solution was measured against blank at 505nm (range 500-540nm). by blank calorimeter was set at zero and then calculation was done as follows:

$$\text{Total cholesterol/concentration of test sample (mg/dl)} = \frac{\text{O.D. of S}}{\text{O.D. of Tc}} \times 200$$

(Cholesterol Immol/L-38.76mg/dl)

(Normal expected values <200 mg/dl)

2. Serum triglycerides (STG): It was estimated by enzymatic procedure of Bucolo and David modified by Trinder to a calorimetric test.

It was estimated by using GPO/POD method with ESPAS (N-Ethyl-N-Sulfopropyl-N-anisidine) utilizing the kit provided by 'Monozyme India Limited'.

Procedure :

Three test tubes were taken and labelled as test (T), standard (s) and blank (b) and then following steps were undertaken:

	Test (T)	Standard (s)	Blank (b)
Enzyme reagent (1)	1.0ml	1.0ml	1.0ml
Triglyceride standard (200mg%)		0.01ml (10µl)	
Serum	0.01ml (10µl)		

Contents of all the tubes were mixed well and then incubated latroom temperature for 15 minutes.

Optical density (O.D.) of each solution was measured against blank at 546nm (range 540-560). By blank calorimeter was set at zero and then calculation were done as follows.

Serum triglyceride (mg/dl) = $\frac{\text{O.D. of T}}{\text{O.D. of S}}$ x 200

(or conversion in mmol/l= mg/dl x 0.0114mg/dl)

(normal expected value <150mg/dl)

3. High density lipoprotein cholesterol (HDL-c) was estimated by precipitating non HDL-c using phosphotungstic acid and magnesium ions. After precipitation, serum was centrifuged and HDL-c was estimated in the supernatant by enzymatic method using cholesterol esterase, cholesterol oxidase, peroxidase, 4-amino antipyrine and phenol.

Estimation of HDL-c was carried out in two steps. By the kit provided by 'Monozyme India Limited'.

(a) 1st step

In a centrifuge tube following substances were taken :

Serum	0.2ml
Precipitating reagent (2)	0.3ml

Contents were mixed well and. were kept at room temperature for 5 minutes following which it was centrifuged at 3000rpm for 10 minutes to get a clear supernatant.

(b) 2nd step

Same procedure as for the total cholesterol estimation as described above was followed, only the test sample was changed.

	Test (TH)	Standard (s)	Blank (b)
Enzyme reagent (1)	1.0ml	1.0ml	1.0 ml
Cholesterol standard (3) (200mg%)		0.01ml (10µl)	
Supernatant (from step 1)	0.1ml (10µl)		
Distilled water		0.1 ml	0.1 ml

Similarly as for the total cholesterol the tubes were incubated and the optical density was measured.

Calculation was done as follows:

$$\text{HDL cholesterol (mg/dl)} = \frac{\text{O.D. of TH}}{\text{O.D. of S}} \times 50$$

(normal expected value >40mg/dl)

4. Low density lipoprotein cholesterol and very low density lipoprotein (LDL and VLDL). VLDL-c and LDL-c were calculated by the following formula given by Friedelwald et al I (1972) and Fredrickson DS (1972) respectively.

VLDL –c (mg/dl) = STG/5 (this formula is valid if STG value is <600mg/dl)

LDL –c (mg/dl) = STC - (STG/5+HDL-c

STC – (VLDL-c + HDL-c)

Analysis **:**

Results obtained were analysis statistically by student's t-test (Paried t-test).

Results were compared with each group and then conclusion was drawn.

Observations

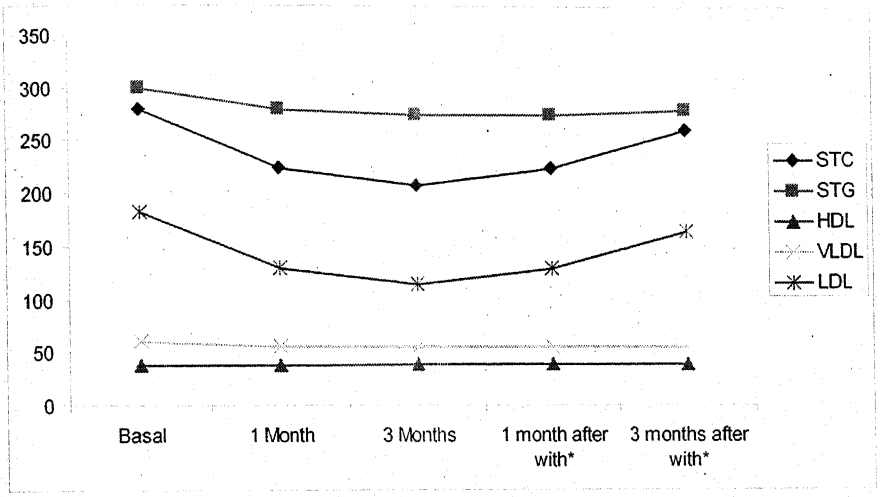
Abbreviations used in the tables are :

STC	Serum total cholesterol
STG	Serum triglyceride
HDL	Serum high density lipoprotein
VLDL	Serum very low density lipoprotein
LDL	Serum low density lipoprotein
LDL/HDL	Ratio of low density lipoprotein to high density lipoprotein
M/F	Male/Female
MI	Myocardial infarction
With*	Withdrawal
CAD	Coronary artery disease
DM	Diabetes Mellitus

ATORVASTATIN GROUP

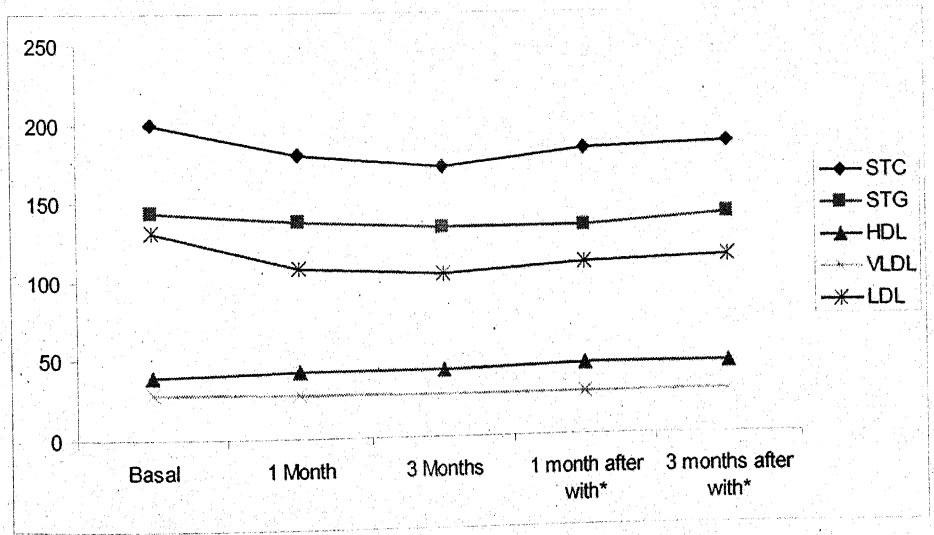
- **Ramesh**
- Age 40 Years/M
- Anterior wall MI

	In mg/dl					
	STC	STG	HDL	VLDL	LDL	LDL/HDL
Basal	280	300	38	60	182	4.8
1 Month	224	280	38	56	130	3.4
3 Months	208	274	39	55	114	2.9
1 month after with*	224	274	39	55	130	3.3
3 months after with*	260	280	39	56	165	4.2



- **Hari Prasad**
- Age 52 Years/M
- Diabetes Mellitus with CAD

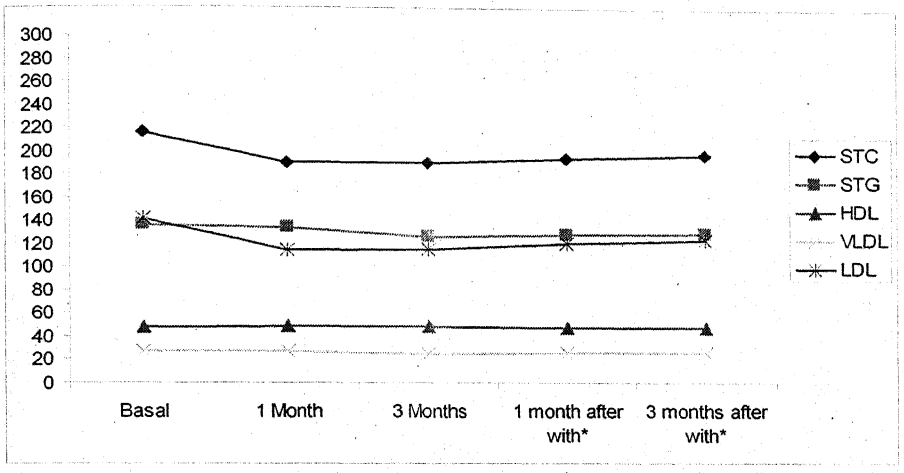
	In mg/dl					
	STC	STG	HDL	VLDL	LDL	LDL/HDL
Basal	200	144	40	29	131	3.2
1 Month	180	138	42	28	108	2.6
3 Months	172	133	42	27	103	2.5
1 month after with*	183	133	45	27	110	2.4
3 months after with*	186	140	45	28	113	2.5



ATORVASTATIN GROUP

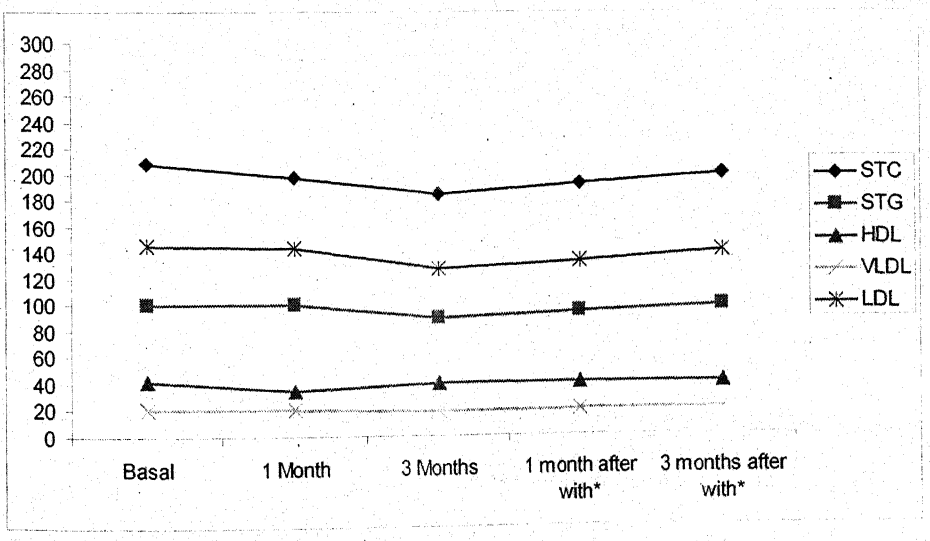
- **Arjun Pal Singh**
- Age 48 Years/M
- Systemic Hypertension

	In mg/dl					
	STC	STG	HDL	VLDL	LDL	LDL/HDL
Basal	216	136	48	27	141	2.9
1 Month	190	134	49	27	114	2.3
3 Months	190	126	49	25	116	2.4
1 month after with*	194	128	47	26	121	2.6
3 months after with*	197	130	47	26	124	2.6



- **Beni Bai**
- Age 64 Years/F
- D.M. with Anteriol wall MI

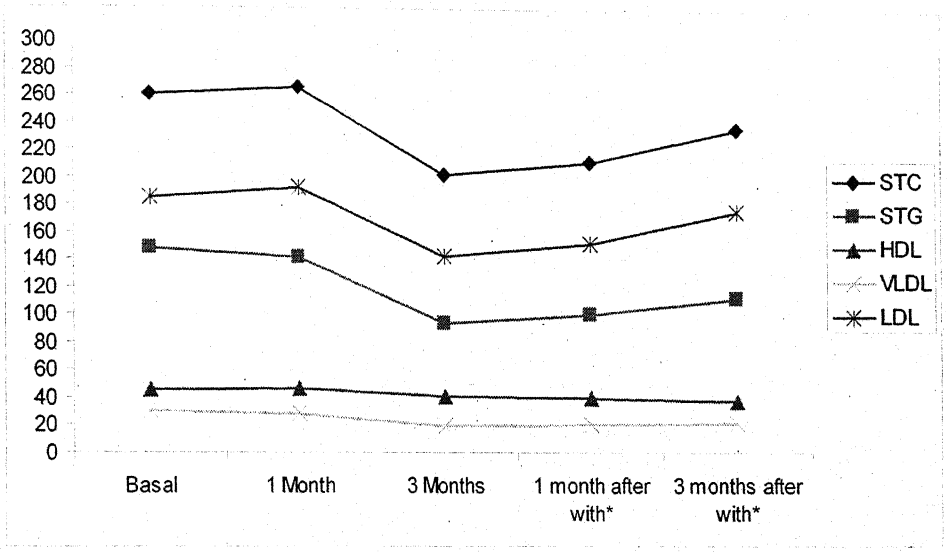
	In mg/dl					
	STC	**STG**	**HDL**	**VLDL**	**LDL**	**LDL/HDL**
Basal	208	100	42	20	146	3.5
1 Month	198	100	35	20	143	4.1
3 Months	185	90	40	18	127	3.2
1 month after with*	192	94	40	19	133	3.3
3 months after with*	200	98	40	20	140	3.5



ATORVASTATIN GROUP

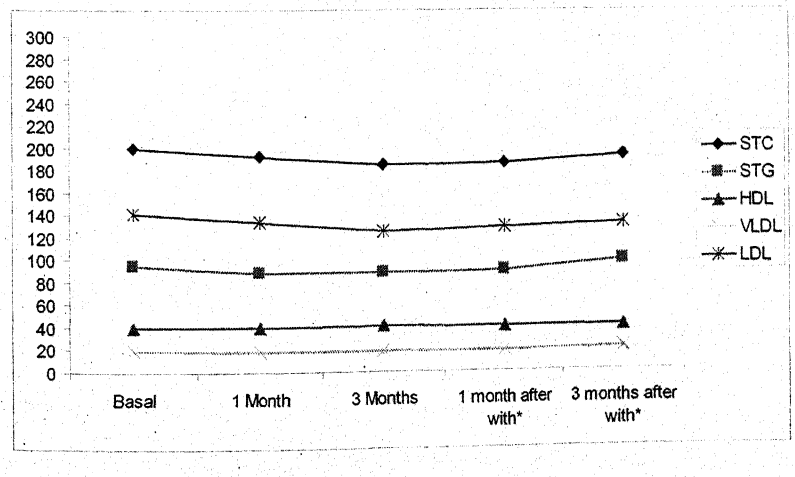
- **Shankar Lal**
- Age 40 Years/M
- Inf. wall MI

	In mg/dl					
	STC	STG	HDL	VLDL	LDL	LDL/HDL
Basal	260	148	45	30	185	4.1
1 Month	266	141	46	28	192	4.2
3 Months	202	94	41	19	142	3.5
1 month after with*	212	100	40	20	152	3.8
3 months after with*	236	112	38	22	176	4.6



- **Indra Dev Gupta**
- Age 54 Years/M
- Unstable angina

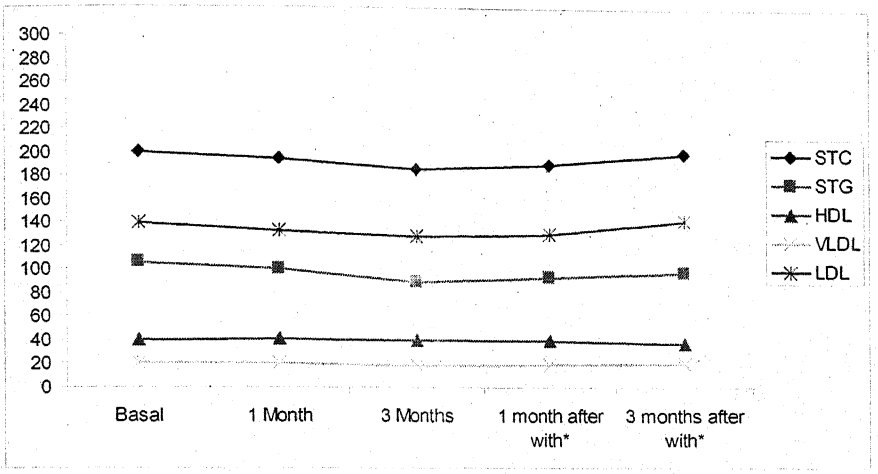
	In mg/dl					
	STC	STG	HDL	VLDL	LDL	LDL/HDL
Basal	200	95	40	19	141	3.5
1 Month	192	88	40	18	134	3.4
3 Months	184	88	41	18	125	3
1 month after with*	186	90	40	18	128	3.2
3 months after with*	192	98	40	20	132	3.3



ATORVASTATIN GROUP

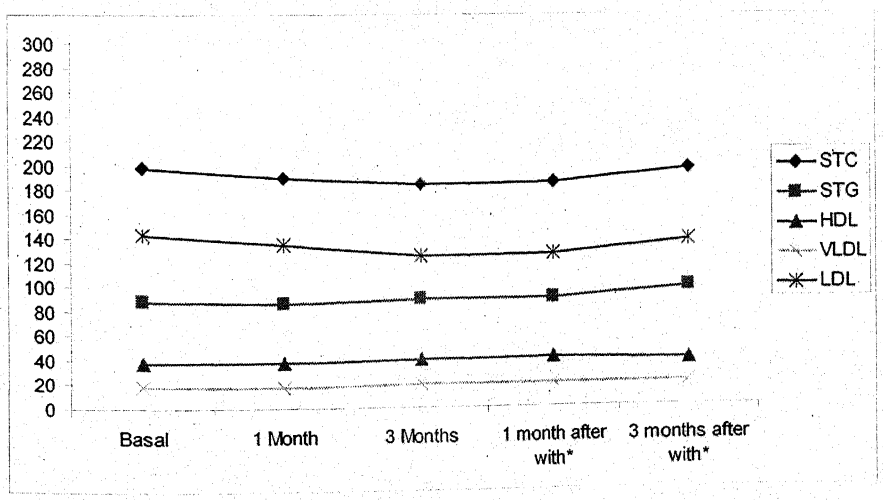
- **Raja Ram**
- Age 44 Years/M
- Anterolateral wall MI

	In mg/dl					
	STC	STG	HDL	VLDL	LDL	LDL/HDL
Basal	200	106	40	21	139	3.5
1 Month	194	100	41	20	133	3.2
3 Months	186	90	40	18	128	3.2
1 month after with*	190	94	40	19	131	3.3
3 months after with*	200	98	38	20	142	3.7



- **Nathu Ram**
- Age 50 Years/M
- Acute Anterior wall MI

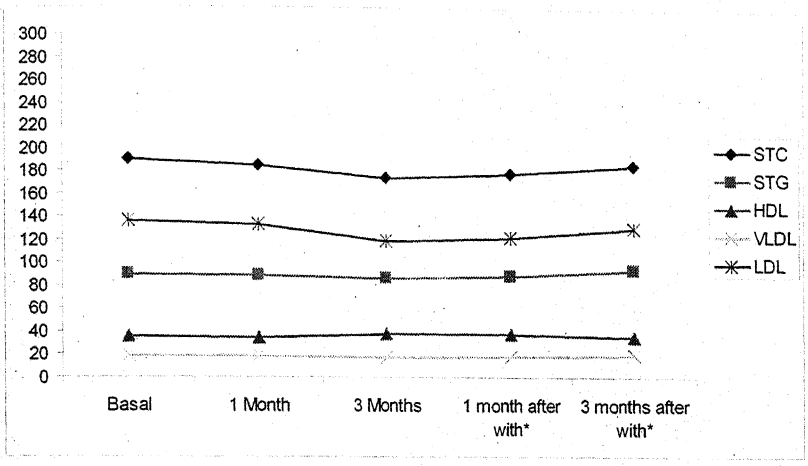
	In mg/dl					
	STC	STG	HDL	VLDL	LDL	LDL/HDL
Basal	199	88	38	18	143	3.8
1 Month	190	86	38	17	135	3.6
3 Months	184	90	40	19	125	3.1
1 month after with*	186	90	41	19	126	3
3 months after with*	196	98	39	20	137	3.5



ATORVASTATIN GROUP

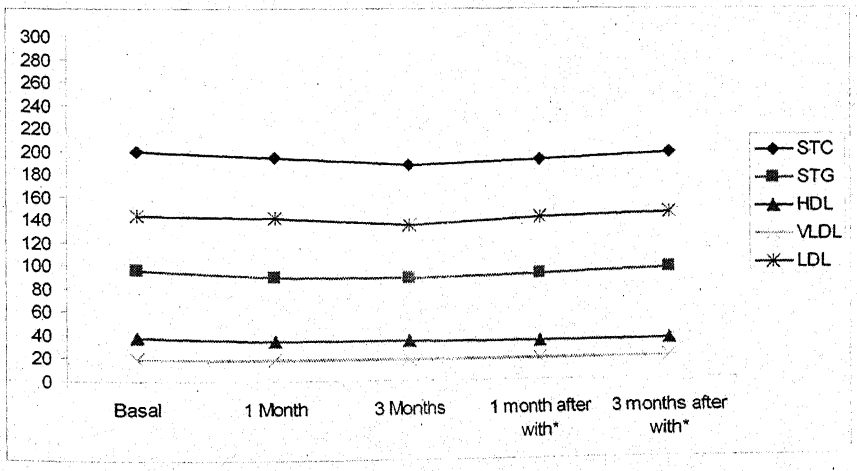
- **Rustam Khan**
- Age 54 Years/M
- Old Inferior wall MI

	In md/dl					
	STC	STG	HDL	VLDL	LDL	LDL/HDL
Basal	190	90	36	18	136	3.8
1 Month	185	88	34	18	133	3.9
3 Months	174	86	38	17	119	3.1
1 month after with*	178	88	38	18	122	3.2
3 months after with*	186	94	36	19	131	3.6



- **Mewa Ram**
- Age 50 Years/M
- Extensive anterior wall MI

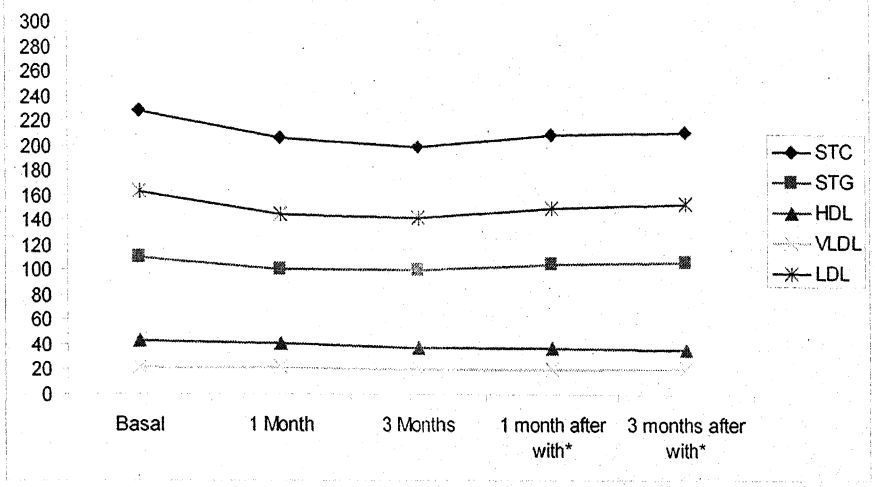
	In mg/dl					
	STC	STG	HDL	VLDL	LDL	LDL/HDL
Basal	200	96	38	19	143	3.8
1 Month	194	90	35	18	141	4
3 Months	188	88	35	18	135	3.9
1 month after with*	192	92	33	18	141	4.3
3 months after with*	198	96	34	19	145	4.3



ATORVASTATIN GROUP

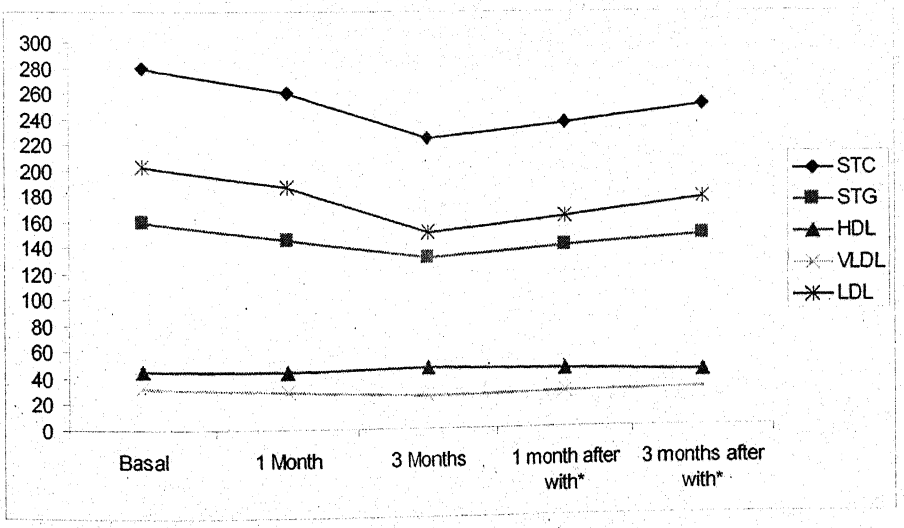
- **Ram Khilawan**
- Age 48 Years/M
- Systemic Hypertension

	In mg/dl					
	STC	STG	HDL	VLDL	LDL	LDL/HDL
Basal	228	110	43	22	163	3.8
1 Month	206	100	41	22	145	3.5
3 Months	200	100	38	20	142	3.7
1 month after with*	210	106	38	21	151	4
3 months after with*	214	108	37	22	155	4.2



- **Kiran Singh**
- Age 35 Years/F
- Systemic Hypertension

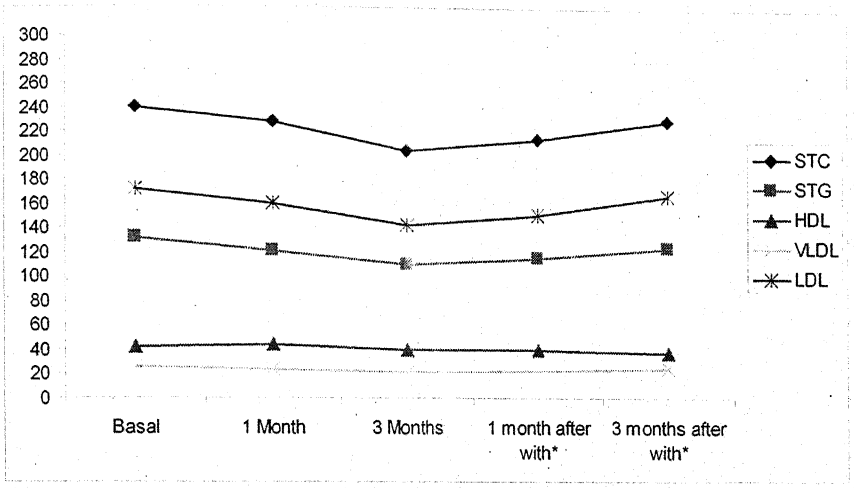
	In mg/dl					
	STC	STG	HDL	VLDL	LDL	LDL/HDL
Basal	280	160	45	32	203	4.5
1 Month	260	146	44	29	187	4.3
3 Months	224	132	47	26	151	3.2
1 month after with*	236	140	45	28	163	3.6
3 months after with*	250	148	43	30	177	4.1



ATORVASTATIN GROUP

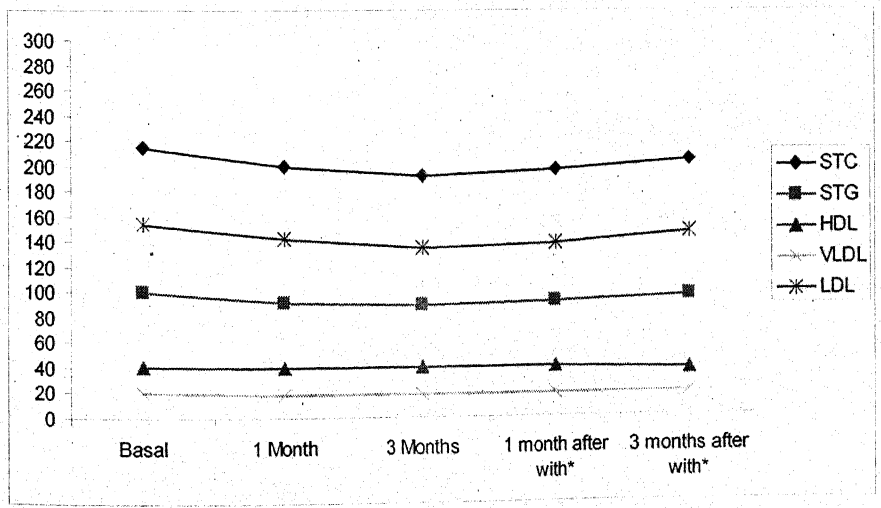
- **Bhagwan Das**
- Age 48 Years/M
- Type I - D.M.

	In mg/dl					
	STC	STG	HDL	VLDL	LDL	LDL/HDL
Basal	240	132	42	26	172	4.1
1 Month	228	121	44	24	160	3.6
3 Months	204	110	40	22	142	3.6
1 month after with*	214	116	40	23	151	3.8
3 months after with*	230	124	38	25	167	4.4



- **Vimla Saxena**
- Age 46 Years/F
- D.M. with CAD

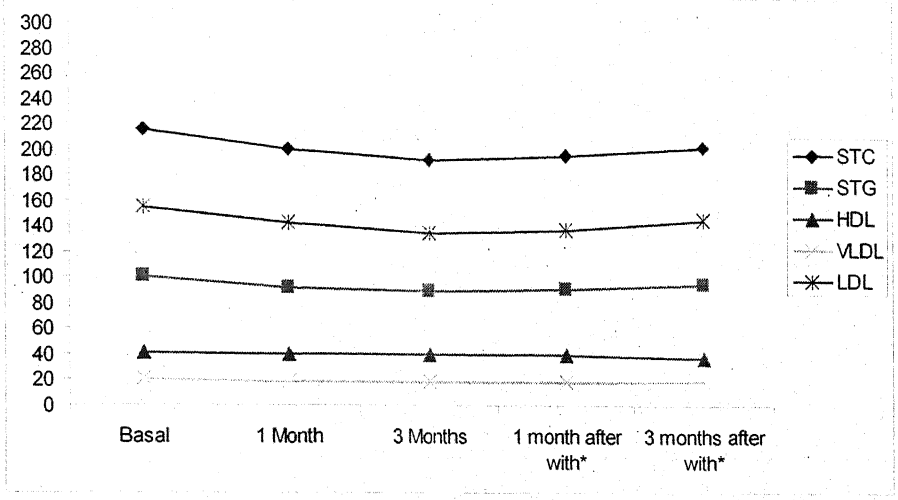
	In mg/dl					
	STC	STG	HDL	VLDL	LDL	LDL/HDL
Basal	215	100	41	20	154	3.8
1 Month	200	92	40	18	142	3.6
3 Months	192	90	40	18	135	3.4
1 month after with*	196	92	40	18	138	3.5
3 months after with*	204	96	38	19	147	3.9



ATORVASTATIN GROUP

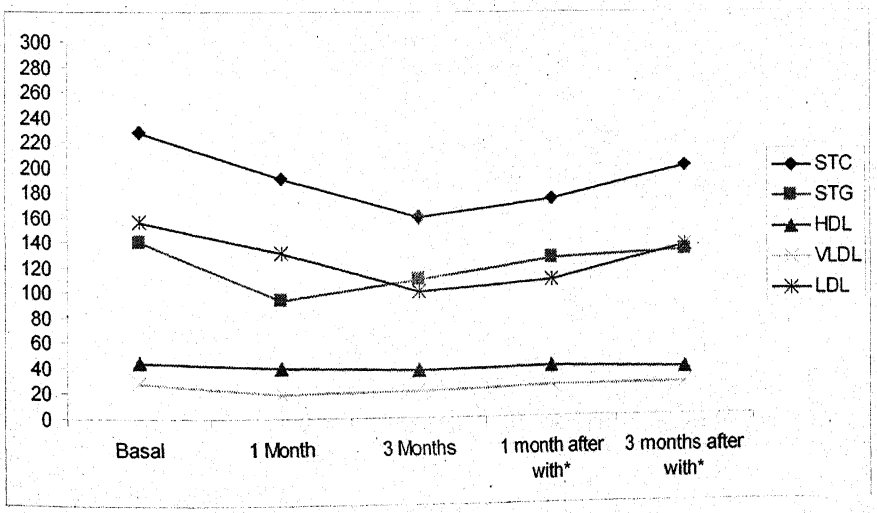
- **Balasi Ram**
- Age 54 Years/M
- Inferior wall MI

	In mg/dl					
	STC	**STG**	**HDL**	**VLDL**	**LDL**	**LDL/HDL**
Basal	198	100	40	20	138	3.5
1 Month	190	98	40	20	130	3.3
3 Months	180	90	40	18	122	3.1
1 month after with*	186	94	39	19	128	3.3
3 months after with*	192	96	39	19	136	3.5



- **Shiv Charan**
- Age 32 Years/F
- D.M.

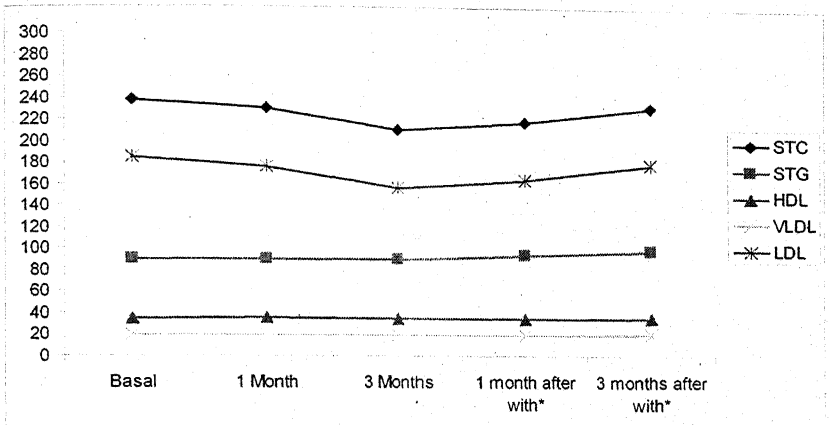
	In mg/dl					
	STC	**STG**	**HDL**	**VLDL**	**LDL**	**LDL/HDL**
Basal	228	140	44	28	156	3.5
1 Month	191	94	40	19	132	3.3
3 Months	160	110	38	22	100	2.6
1 month after with*	174	126	40	25	109	2.7
3 months after with*	200	132	38	26	136	2.6



ATORVASTATIN GROUP

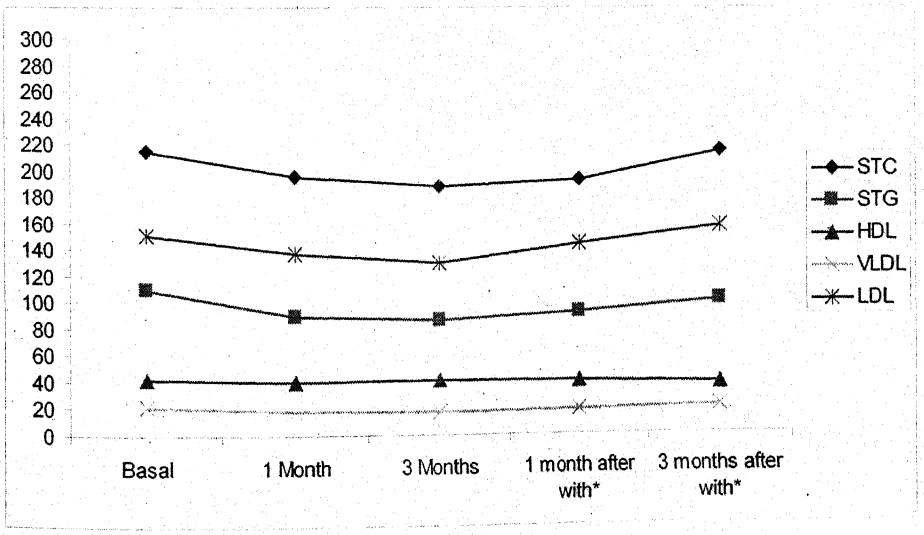
- **N.P. Janardan**
- Age 50 Years/M
- Systemic Hypertension

	In mg/dl					
	STC	STG	HDL	VLDL	LDL	LDL/HDL
Basal	237	90	35	19	184	5.3
1 Month	230	90	36	19	176	4.9
3 Months	210	90	35	19	157	4.5
1 month after with*	218	94	35	19	164	4.7
3 months after with*	232	98	36	20	179	5.4



- **Yashwant Nagar**
- Age 48 Years/M
- D.M.

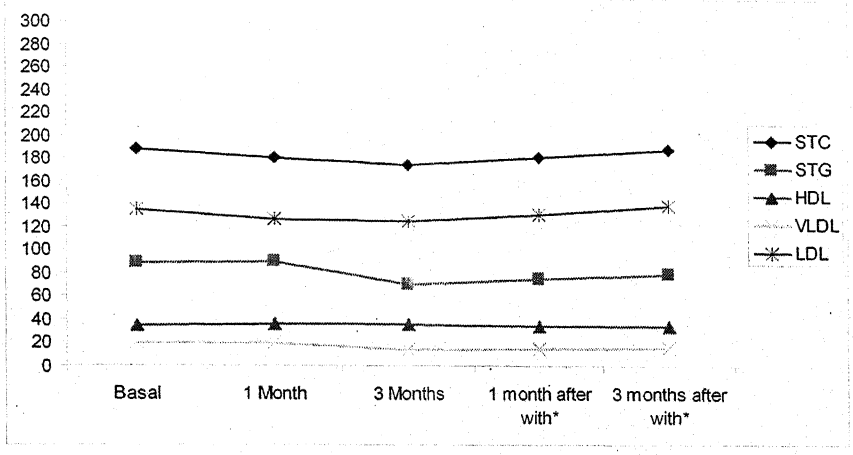
	In mg/dl					
	STC	STG	HDL	VLDL	LDL	LDL/HDL
Basal	215	110	42	22	151	3.6
1 Month	195	90	40	18	137	3.4
3 Months	188	86	41	17	130	3.1
1 month after with*	192	92	40	18	144	3.6
3 months after with*	214	100	38	20	156	4.1



ATORVASTATIN GROUP

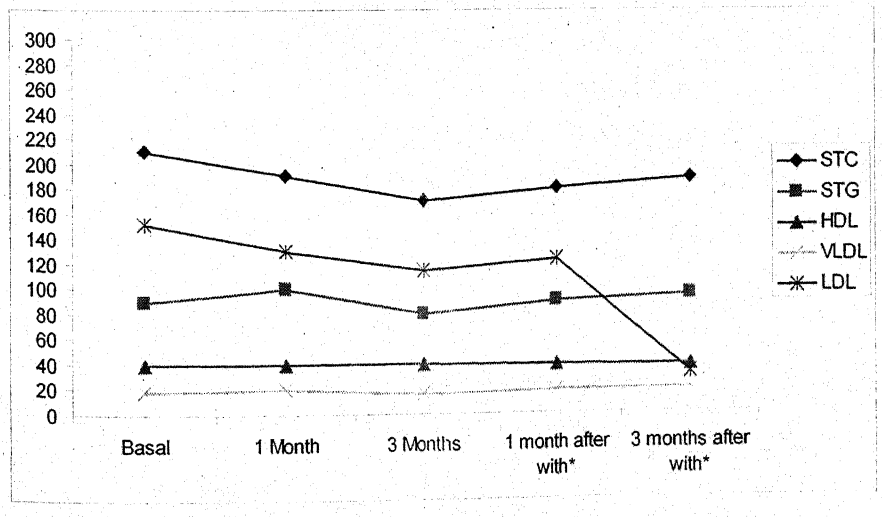
- **Laxman Singh**
- Age 44 Years/M
- Antero Lateral wall MI

	In mg/dl					
	STC	STG	HDL	VLDL	LDL	LDL/HDL
Basal	188	89	35	19	135	3.9
1 Month	180	90	36	19	126	3.5
3 Months	175	70	36	14	125	3.5
1 month after with*	182	76	35	15	132	3.8
3 months after with*	190	80	34	16	140	4.1



- **Sharda**
- Age 48 Years/F
- Systemic Hypertension

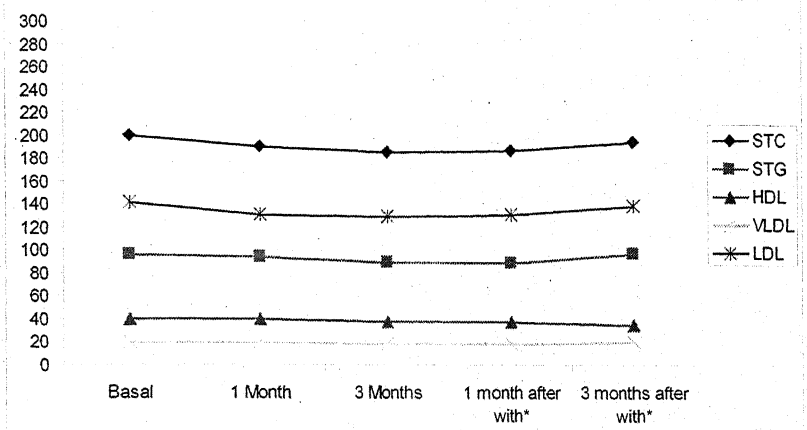
	In mg/dl					
	STC	STG	HDL	VLDL	LDL	LDL/HDL
Basal	210	90	40	18	152	3.8
1 Month	191	100	40	20	131	3.3
3 Months	170	80	40	16	114	2.9
1 month after with*	180	90	39	18	123	3.2
3 months after with*	188	94	38	19	31	3.4



ATORVASTATIN GROUP

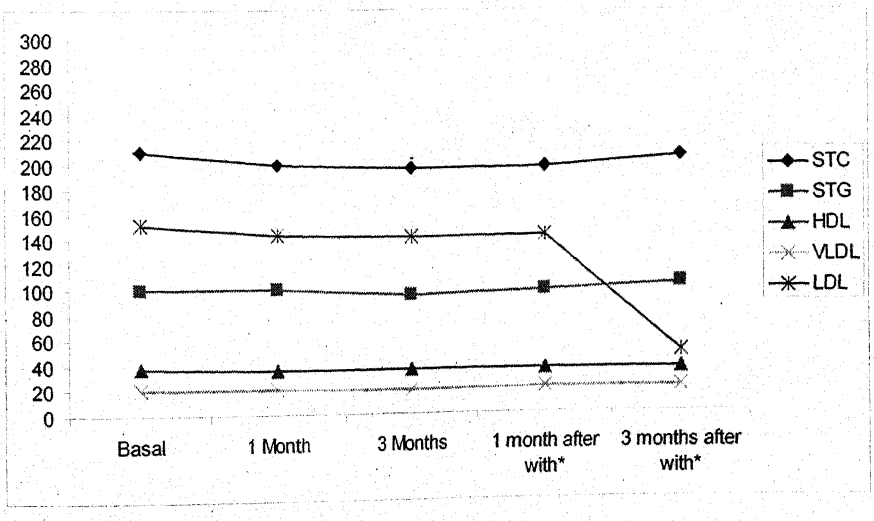
- **Shiv Ram Singh**
- Age 50 Years/M
- Antero Lateral wall ischemia .

	In /mg/dl					
	STC	STG	HDL	VLDL	LDL	LDL/HDL
Basal	200	96	40	19	141	3.5
1 Month	190	94	40	19	131	3.3
3 Months	186	90	38	18	130	3.4
1 month after with*	188	90	38	18	132	3.5
3 months after with*	196	98	36	20	140	3.9



- **Sooraj**
- Age 45 Years/M
- Hypertension

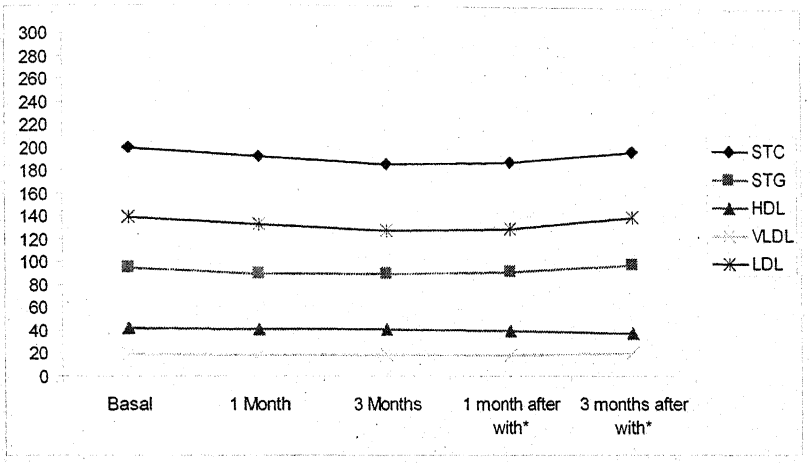
	In mg/dl					
	STC	STG	HDL	VLDL	LDL	LDL/HDL
Basal	210	100	38	20	152	4
1 Month	200	100	36	20	144	4
3 Months	196	95	36	19	141	3.9
1 month after with*	198	98	36	20	142	3.9
3 months after with*	206	104	36	21	49	4.1



ATORVASTATIN GROUP

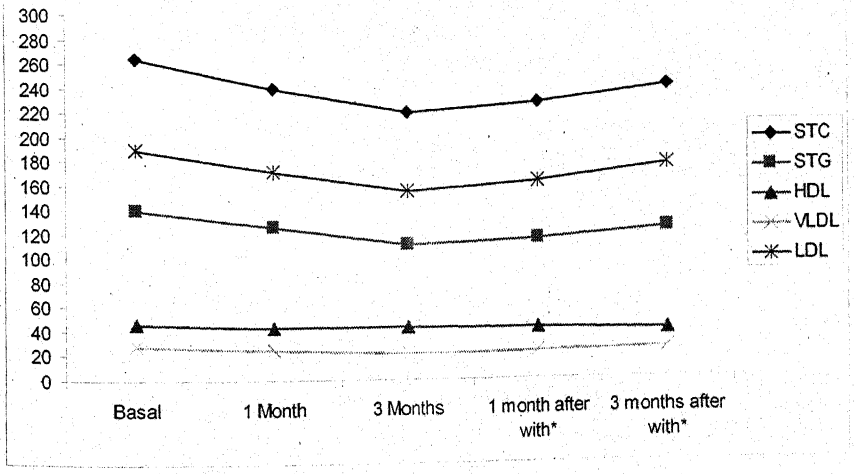
- **Gayatri**
- Age 48 Years/F
- Type II- D.M.

	In mg/dl					
	STC	STG	HDL	VLDL	LDL	LDL/HDL
Basal	200	95	42	19	139	3.3
1 Month	192	90	41	18	133	3.2
3 Months	186	90	41	18	127	3.1
1 month after with*	188	92	40	18	130	3.3
3 months after with*	198	98	38	20	140	3.7



- **N.C. Jain**
- Age 54 Years/M
- Diabetes with CAD

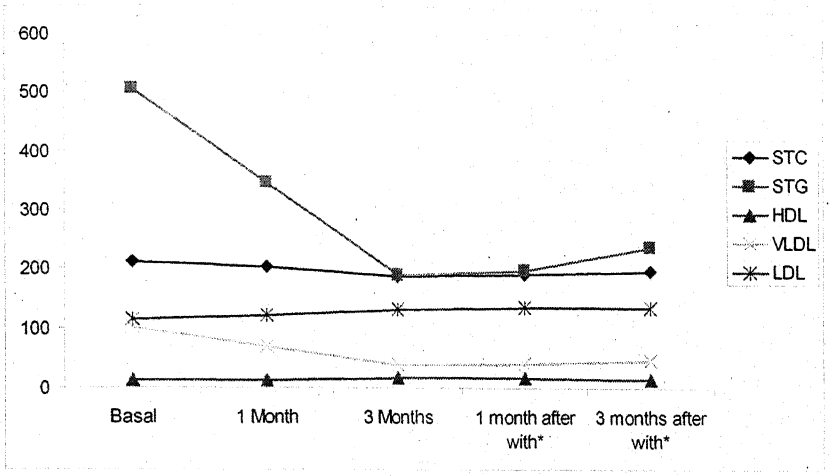
	In mg/dl					
	STC	STG	HDL	VLDL	LDL	LDL/HDL
Basal	264	140	46	28	190	4.1
1 Month	240	126	43	25	172	4
3 Months	220	111	43	22	155	3.6
1 month after with*	228	116	42	23	163	3.9
3 months after with*	242	124	40	25	177	4.4



FENOFIBRATE GROUP

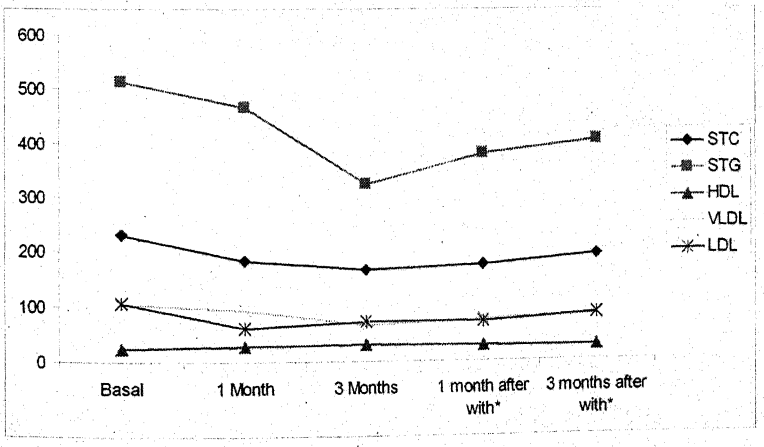
- **Radha Rani**
- Age 40 Years/F
- DM.

	STC	STG	HDL	VLDL	LDL	LDL/HDL
Basal	212	506	12	101	114	9.5
1 Month	202	346	13	69	120	9.2
3 Months	187	190	17	38	132	7.8
1 month after with*	192	198	17	40	135	7.9
3 months after with*	198	240	15	48	135	9



- **Dr. Adarash Shrivastava**
- Age 45 Years/M
- Systemic Hypertension

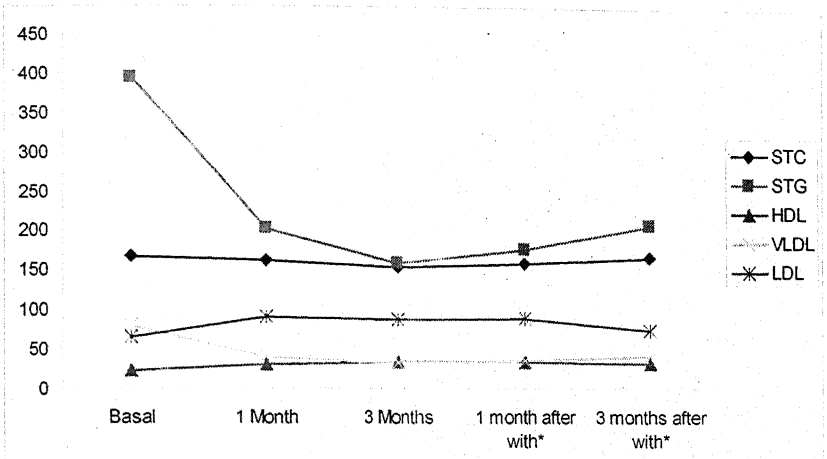
	In mg/dl					
	STC	STG	**HDL**	**VLDL**	**LDL**	**LDL/HDL**
Basal	232	513	23	103	106	4.6
1 Month	183	466	29	93	60	2
3 Months	166	324	30	65	71	2.4
1 month after with*	174	380	28	76	71	2.5
3 months after with*	192	404	26	81	85	2.3



FENOFIBRATE GROUP

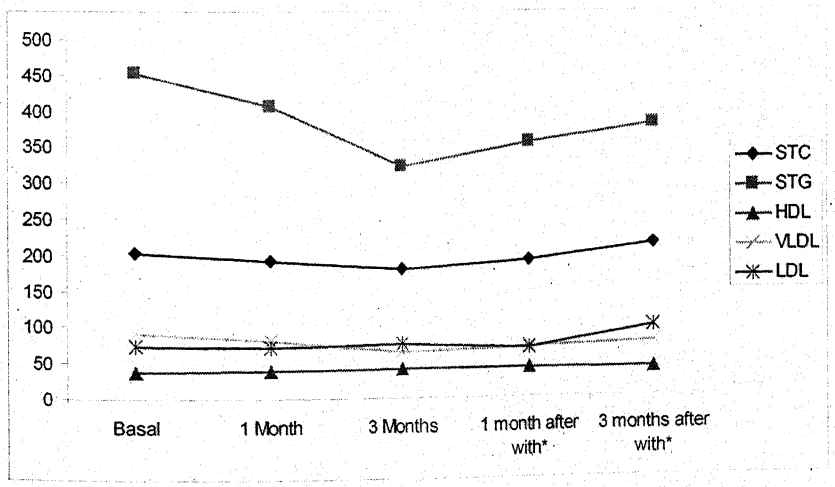
- **R.K. Ojha**
- Age 42 Years/M
- CAD

	In mg/dl					
	STC	STG	HDL	VLDL	LDL	LDL/HDL
Basal	166	394	23	79	64	2.8
1 Month	162	203	30	41	91	3
3 Months	154	158	34	32	88	2.6
1 month after with*	158	176	34	35	89	2.6
3 months after with*	166	208	33	42	75	2.3



- **K.C. Pandey**
- Age 42 Years/M
- DM with Systemic Hypertension

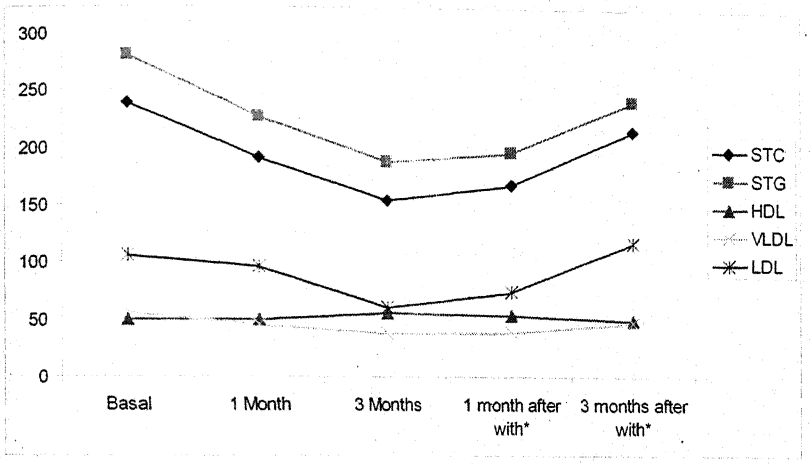
	In mg/dl					
	STC	STG	HDL	VLDL	LDL	LDL/HDL
Basal	203	454	38	91	74	1.9
1 Month	192	407	39	81	72	1.8
3 Months	180	322	41	64	75	1.1
1 month after with*	191	354	41	71	69	1.7
3 months after with*	212	380	39	76	97	2.5



FENOFIBRATE GROUP

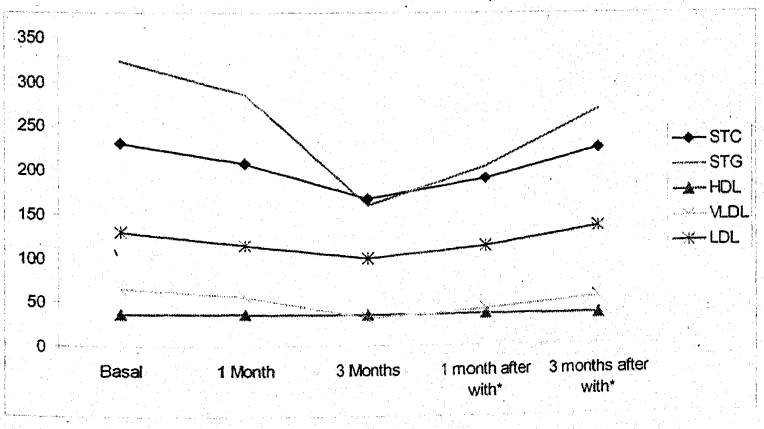
- **Mohd. Jalal**
- Age 45 Years/M
- Ant wall MI

	In mg/dl					
	STC	STG	HDL	VLDL	LDL	LDL/HDL
Basal	238	281	50	56	106	2.1
1 Month	191	227	50	45	96	1.9
3 Months	154	188	56	38	60	1.1
1 month after with*	168	196	54	39	75	1.4
3 months after with*	216	242	50	48	118	2.7



- **Mr. M.S. Khan**
- Age 65 Years/M
- Systemic Hypertension

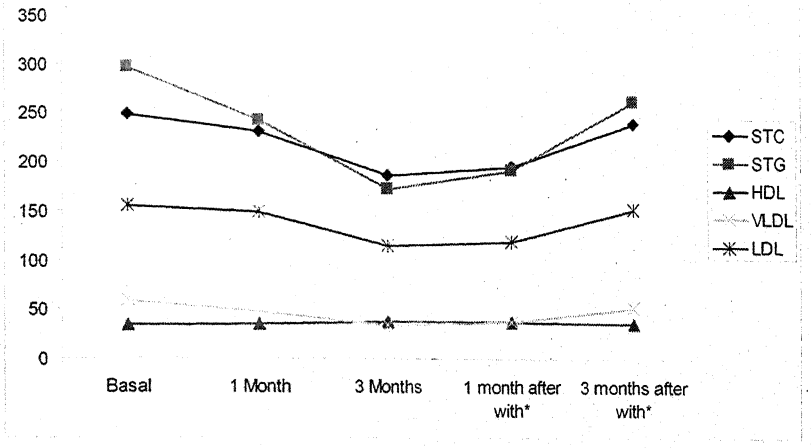
	In mg/dl					
	STC	STG	HDL	VLDL	LDL	LDL/HDL
Basal	231	323	36	65	130	3.6
1 Month	208	286	36	57	115	3.2
3 Months	167	160	35	32	100	2.9
1 month after with*	190	204	36	41	113	3.1
3 months after with*	224	268	35	54	135	3.9



FENOFIBRATE GROUP

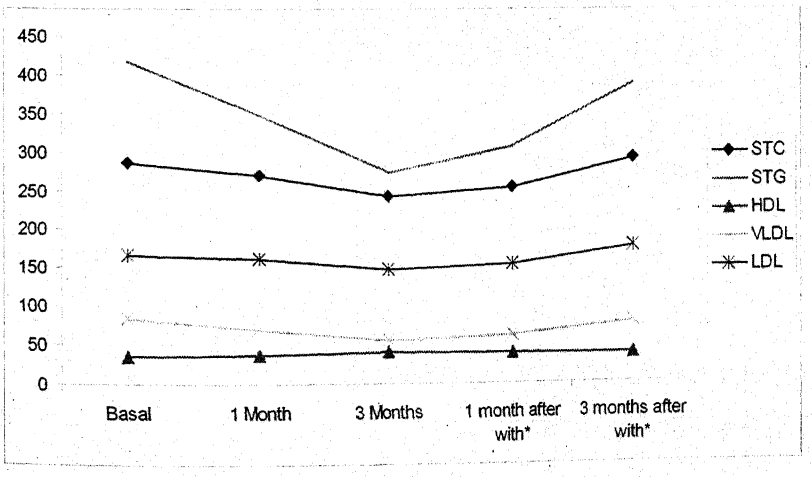
- **Shiv Khare**
- Age 50 Years/M
- CAD

	In mg/dl					
	STC	STG	HDL	VLDL	LDL	LDL/HDL
Basal	248	296	34	59	155	4.6
1 Month	231	242	35	48	148	4.2
3 Months	186	172	38	34	114	3
1 month after with*	196	192	38	38	120	3.1
3 months after with*	242	264	36	53	153	4.3



- **Ram Bihari**
- Age 48 Years/M
- DM Systemic Hypertension

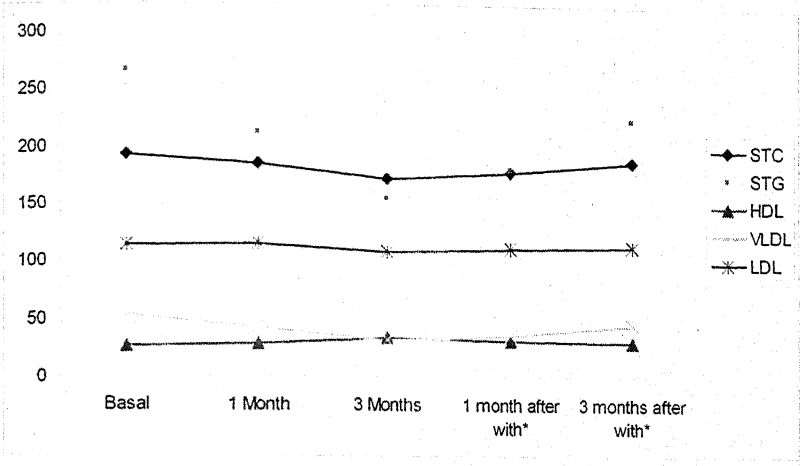
	In mg/dl					
	STC	STG	HDL	VLDL	LDL	LDL/HDL
Basal	286	418	36	84	166	4.6
1 Month	270	348	38	70	162	4.3
3 Months	242	274	40	55	147	3.7
1 month after with*	254	308	39	62	153	3.9
3 months after with*	292	388	37	78	177	4.8



FENOFIBRATE GROUP

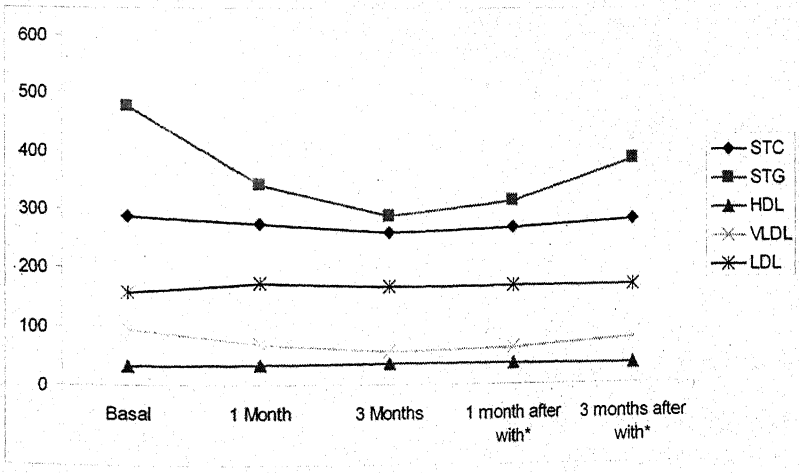
- **Lalta Prasad**
- Age 40 Years/M
- Anterior wall MI

	In mg/dl					
	STC	STG	HDL	VLDL	LDL	LDL/HDL
Basal	192	266	26	53	113	4.3
1 Month	184	212	28	42	114	4.1
3 Months	172	154	33	31	108	3.3
1 month after with*	178	180	31	36	111	3.6
3 months after with*	188	224	30	45	113	3.8



- **Veer Singh**
- Age 54 Years/M
- Systemic Hypertension

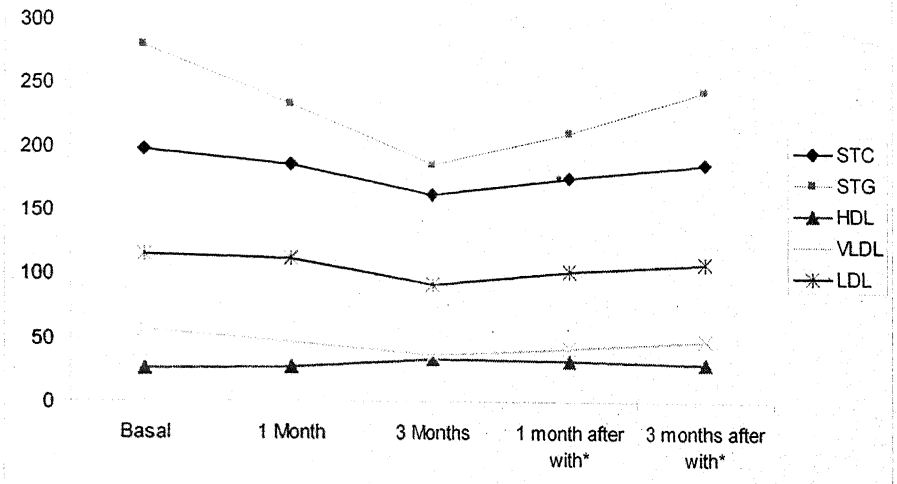
	In mg/dl					
	STC	STG	HDL	VLDL	LDL	LDL/HDL
Basal	286	478	33	96	157	4.8
1 Month	274	342	34	68	172	5.1
3 Months	260	286	37	57	166	4.5
1 month after with*	268	314	36	63	169	4.7
3 months after with*	280	384	34	77	169	5



FENOFIBRATE GROUP

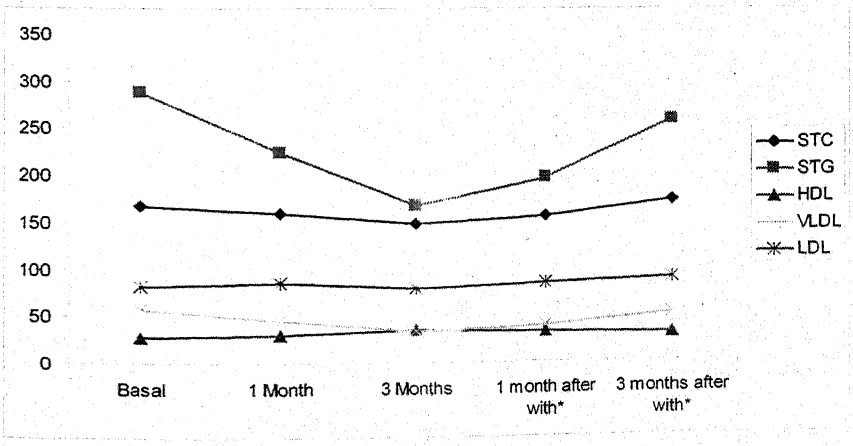
- **Prabha Devi**
- Age 55 Years/F
- Inferior wall MI

	In mg/dl					
	STC	STG	HDL	VLDL	LDL	LDL/HDL
Basal	196	278	26	56	114	4.4
1 Month	184	232	27	46	111	4.1
3 Months	162	186	33	37	92	2.8
1 month after with*	176	212	32	42	102	3.2
3 months after with*	188	246	30	49	109	3.6



- **Uma Shanker**
- Age 60 Years/M
- D.M. with CAD

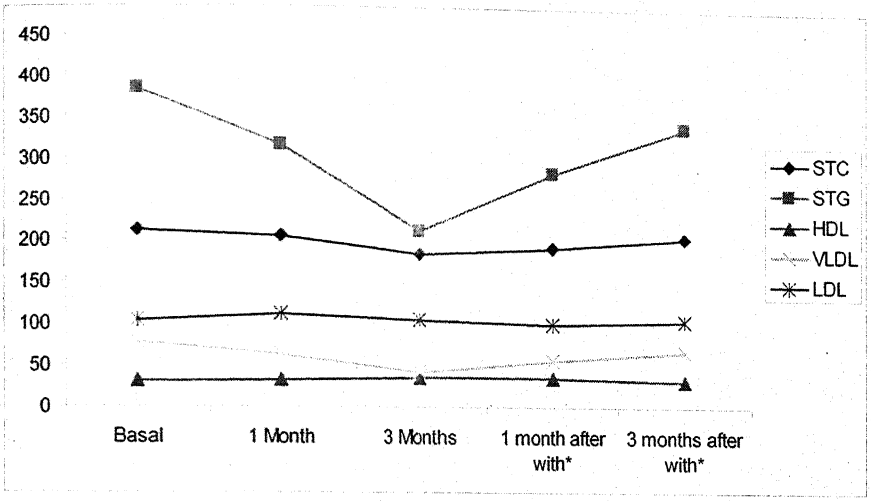
	In mg/dl					
	STC	STG	HDL	VLDL	LDL	LDL/HDL
Basal	168	288	28	58	82	2.9
1 Month	160	224	30	45	85	2.8
3 Months	148	168	35	34	79	2.3
1 month after with*	156	196	33	39	84	2.5
3 months after with*	172	258	30	52	90	3



FENOFIBRATE GROUP

- **Ramachal**
- Age 45 Years/M
- Ant. wall MI

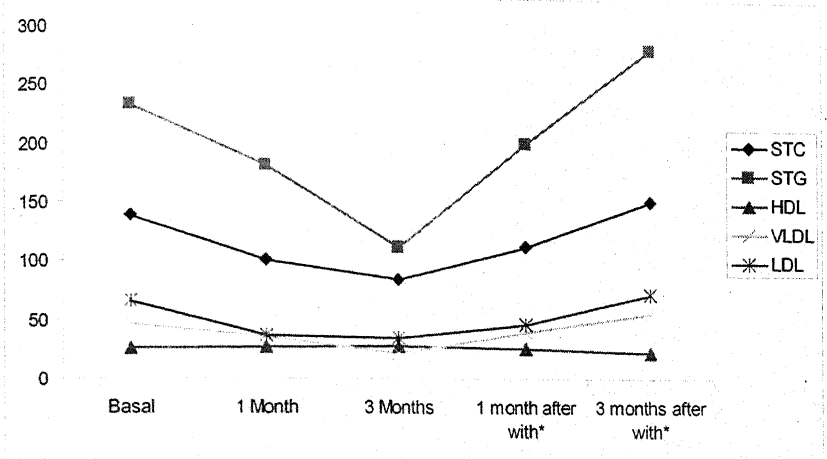
	In mg/dl					
	STC	STG	HDL	VLDL	LDL	LDL/HDL
Basal	212	384	31	77	104	3.4
1 Month	206	316	32	63	111	3.5
3 Months	184	212	36	42	106	2.9
1 month after with*	192	284	35	57	100	2.9
3 months after with*	206	340	33	68	105	3.2



NIACIN GROUP

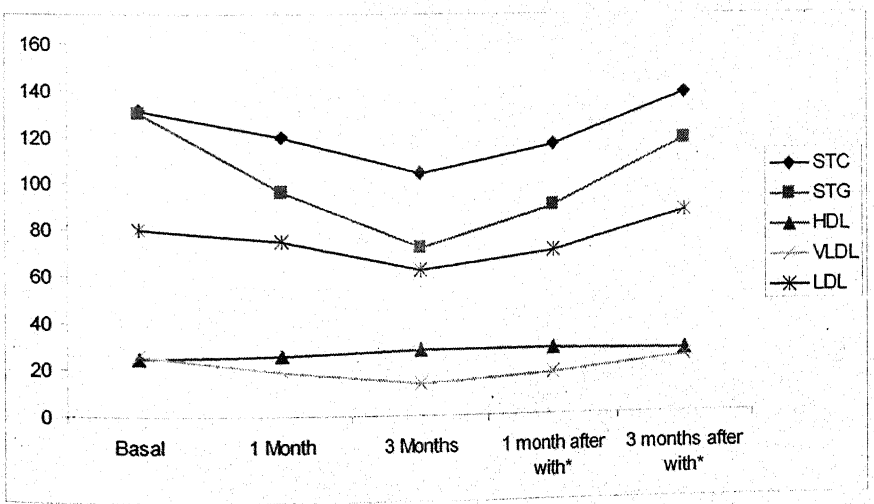
- **Rameshwar**
- Age 40 Years/M
- Inferior wall MI

	In mg/dl					
	STC	STG	HDL	VLDL	LDL	LDL/HDL
Basal	138	232	26	46	66	2.5
1 Month	100	180	27	36	37	1.4
3 Months	84	111	28	22	34	1.21
1 month after with*	112	200	26	40	46	1.8
3 months after with*	151	281	23	56	72	3.1



- **Hari Babu Sharma**
- Age 50 Years/M
- Inf. wall MI

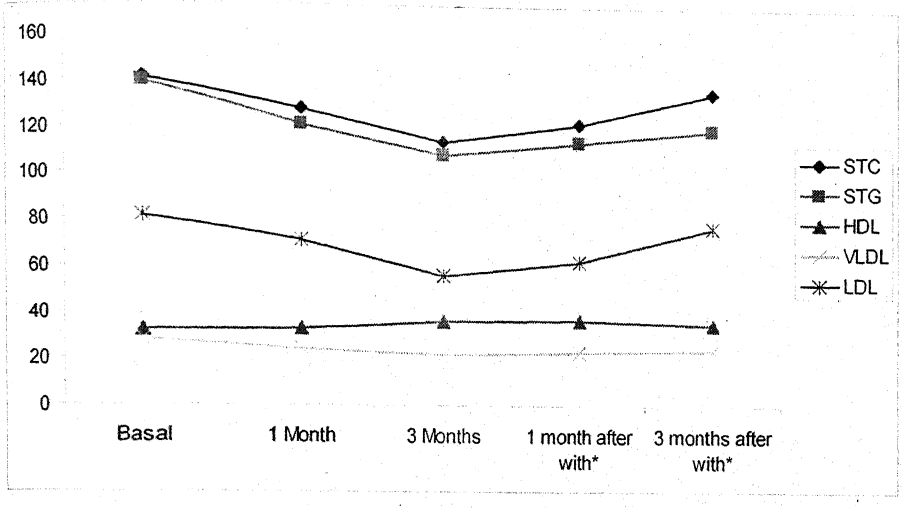
	In mg/dl					
	STC	STG	HDL	VLDL	LDL	LDL/HDL
Basal	131	130	25	26	80	3.2
1 Month	120	96	26	19	75	2.9
3 Months	104	72	28	14	62	2.2
1 month after with*	116	90	28	18	70	2.5
3 months after with*	138	118	27	24	87	3.2



NIACIN GROUP

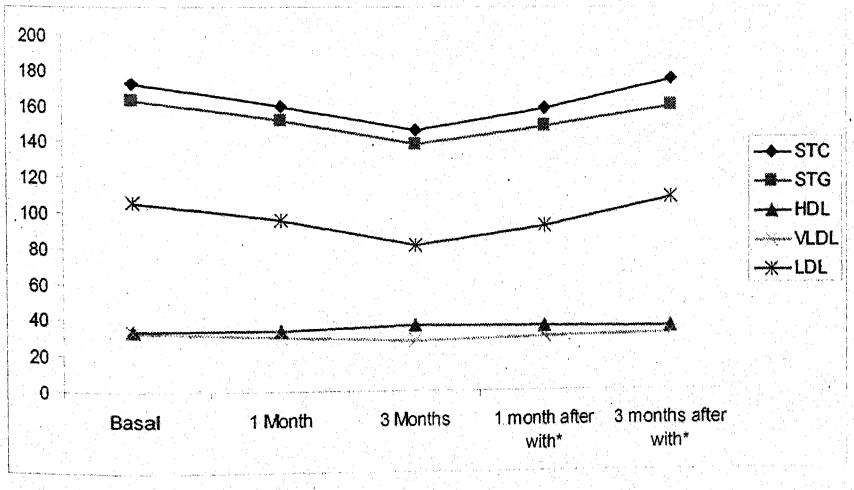
- **Ramesh Chand**
- Age 55 Years/M
- Inf wall MI

	In mg/dl					
	STC	STG	HDL	VLDL	LDL	LDL/HDL
Basal	141	139	32	28	81	2.5
1 Month	128	121	33	24	71	2.2
3 Months	114	108	36	22	56	1.6
1 month after with*	122	114	37	23	62	1.7
3 months after with*	136	120	35	24	77	2.2



- **Om Prakah**
- Age 50 Years/M
- CAD

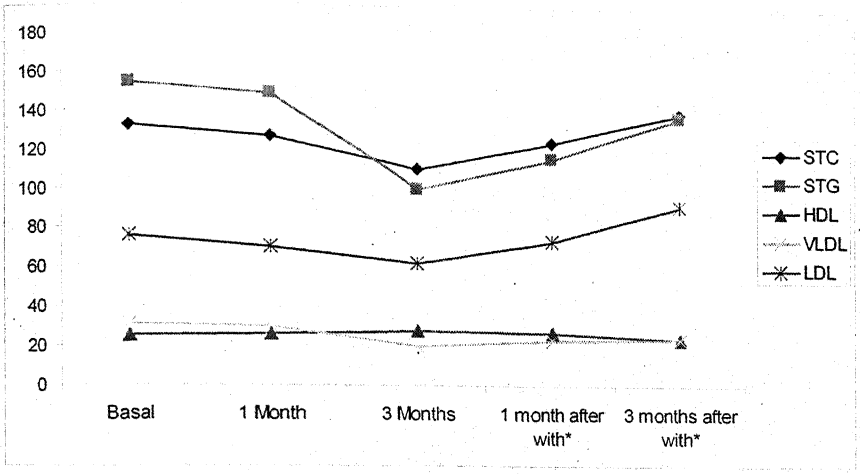
	In mg/dl					
	STC	STG	HDL	VLDL	LDL	LDL/HDL
Basal	173	163	34	33	106	3.1
1 Month	160	152	34	30	96	2.8
3 Months	146	138	37	28	81	2.2
1 month after with*	158	148	36	30	92	2.6
3 months after with*	175	160	35	32	108	3.1



NIACIN GROUP

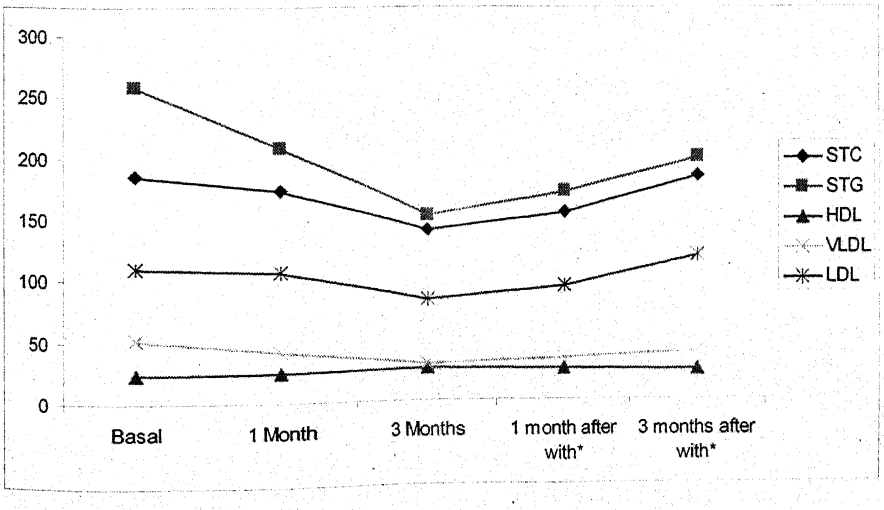
- **Yashwant Singh**
- Age 55 Years/M
- CAD

	In mg/dl					
	STC	**STG**	**HDL**	**VLDL**	**LDL**	**LDL/HDL**
Basal	132	154	25	31	76	3
1 Month	126	148	26	30	70	2.7
3 Months	110	100	28	20	62	2.2
1 month after with*	124	116	27	23	74	2.7
3 months after with*	140	138	24	24	92	3.8



- **P.V. Swami**
- Age 68 Years/M
- CAD

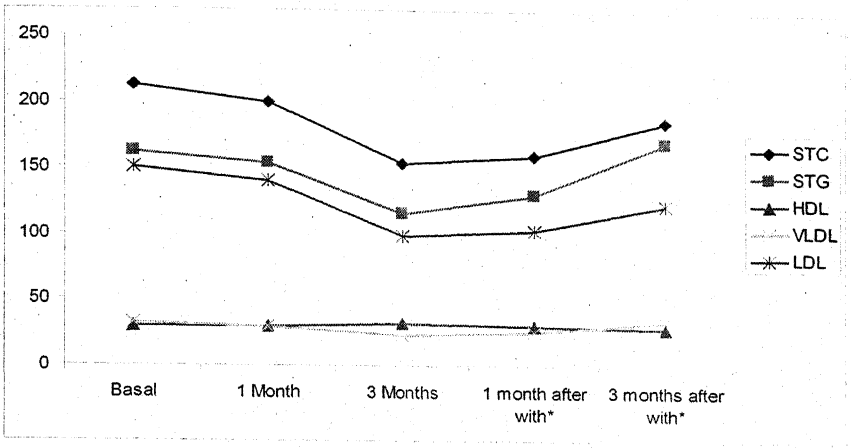
	In mg/dl					
	STC	STG	HDL	VLDL	LDL	LDL/HDL
Basal	186	258	24	52	110	4.4
1 Month	174	208	25	42	107	4.3
3 Months	140	152	27	30	83	3.1
1 month after with*	154	172	26	34	94	3.6
3 months after with*	184	200	25	40	119	4.8



NIACIN GROUP

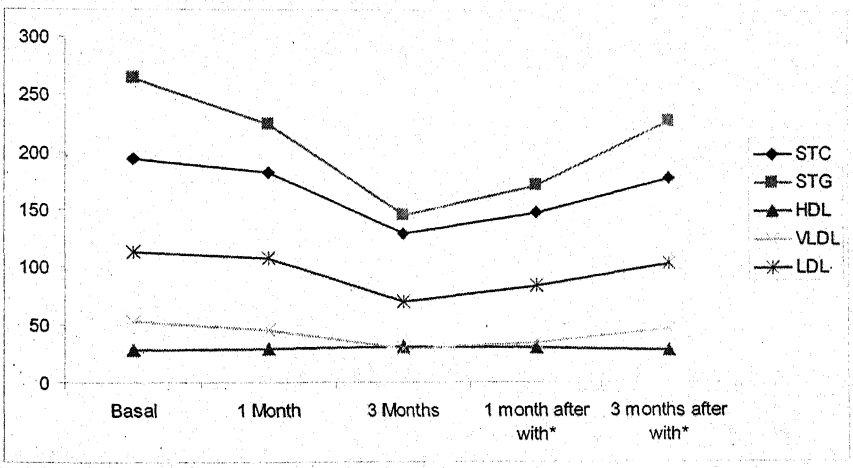
- **Dinesh**
- Age 32 Years/M
- Type I - DM

	In mg/dl					
	STC	STG	HDL	VLDL	LDL	LDL/HDL
Basal	212	162	30	32	150	5
1 Month	200	154	30	30	140	4.7
3 Months	154	116	32	23	99	3.1
1 month after with*	160	130	31	26	103	3.3
3 months after with*	186	170	29	34	123	4.3



- **Moti Ram**
- Age 52 Years/M
- Systemic Hypertension

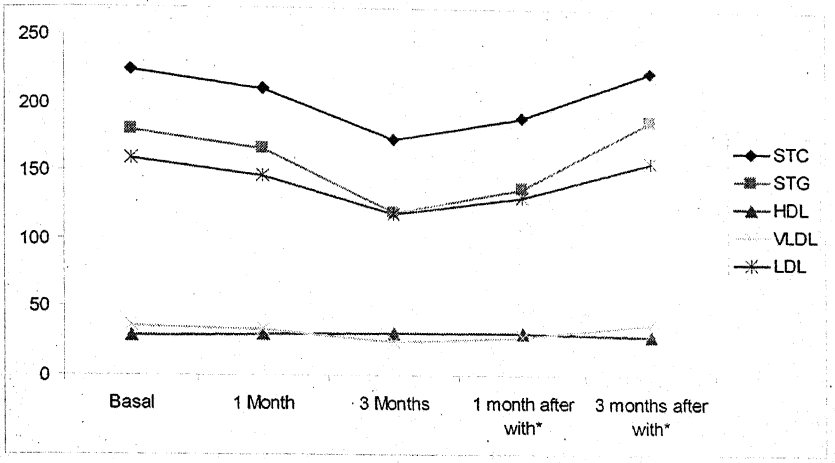
	In/mg/dl					
	STC	STG	HDL	VLDL	LDL	LDL/HDL
Basal	194	264	28	53	113	4
1 Month	182	224	29	45	108	3.7
3 Months	130	146	31	29	70	2.3
1 month after with*	148	172	30	34	84	2.8
3 months after with*	178	228	28	46	104	3.7



NIACIN GROUP

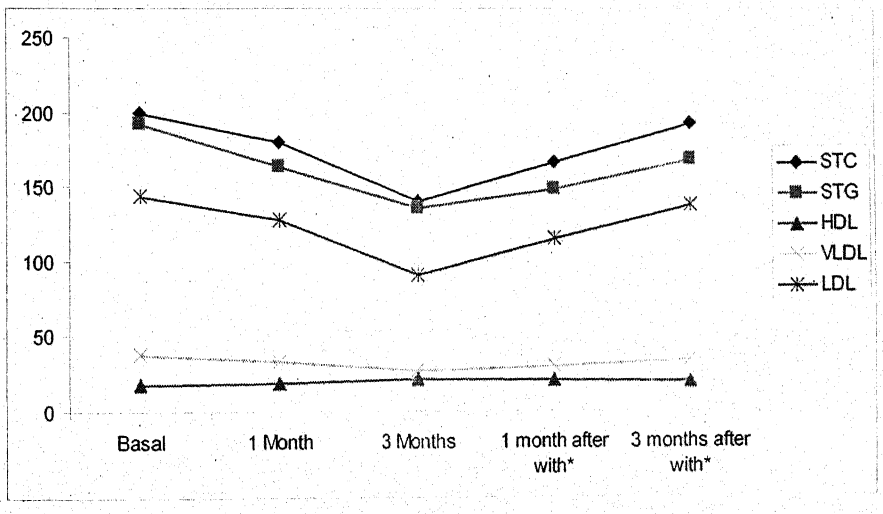
- **Shreen**
- Age 50 Years/F
- DM with CAD

	In mg/dl					
	STC	STG	HDL	VLDL	LDL	LDL/HDL
Basal	224	180	29	36	159	5.5
1 Month	210	166	30	33	147	4.9
3 Months	174	120	31	24	119	3.8
1 month after with*	190	138	31	28	131	4.2
3 months after with*	224	188	29	38	157	5.4



- **Avtar Singh**
- Age 52 Years/M
- Inf. wall ischemia

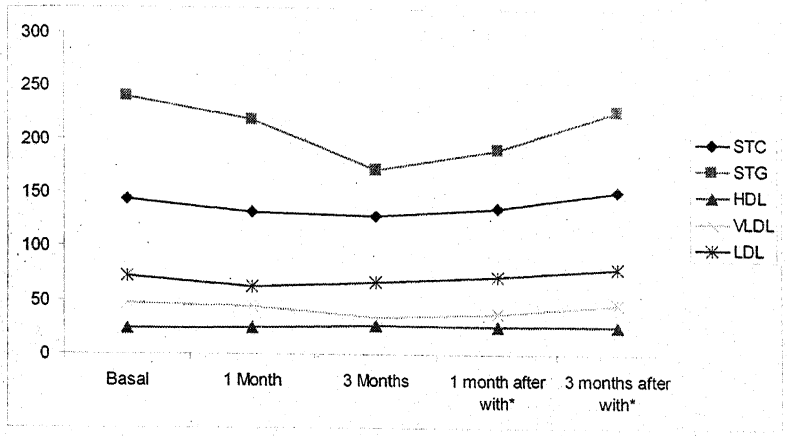
	In mg/dl					
	STC	STG	HDL	VLDL	LDL	LDL/HDL
Basal	200	192	18	38	144	8
1 Month	180	164	19	33	128	6.7
3 Months	140	136	22	27	91	4.3
1 month after with*	166	148	21	30	115	5.5
3 months after with*	192	168	20	34	138	6.9



NIACIN GROUP

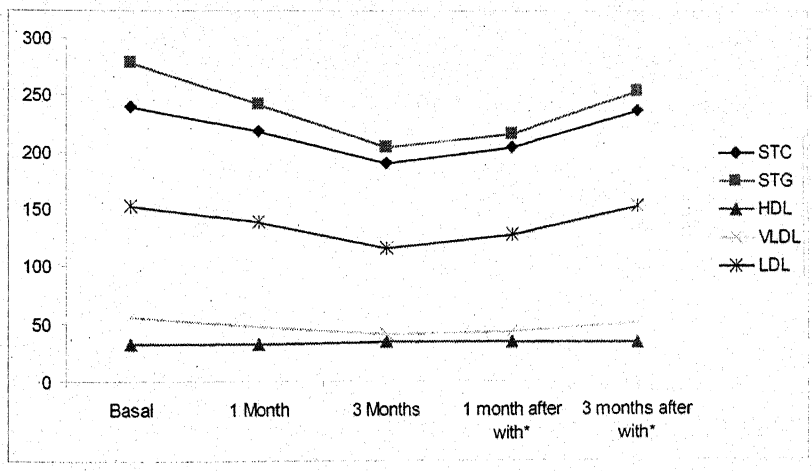
- **Kamal**
- Age 28 Years/M
- Type -I Diabtes Mellitus

	In mg/dl					
	STC	STG	HDL	VLDL	LDL	LDL/HDL
Basal	144	240	24	48	72	3
1 Month	132	218	25	44	63	2.5
3 Months	128	172	27	34	67	2.5
1 month after with*	136	191	26	38	72	2.8
3 months after with*	152	228	26	46	80	3



- **K.K. Kulssratha**
- Age 48 Years/M
- Systemic Hypertension

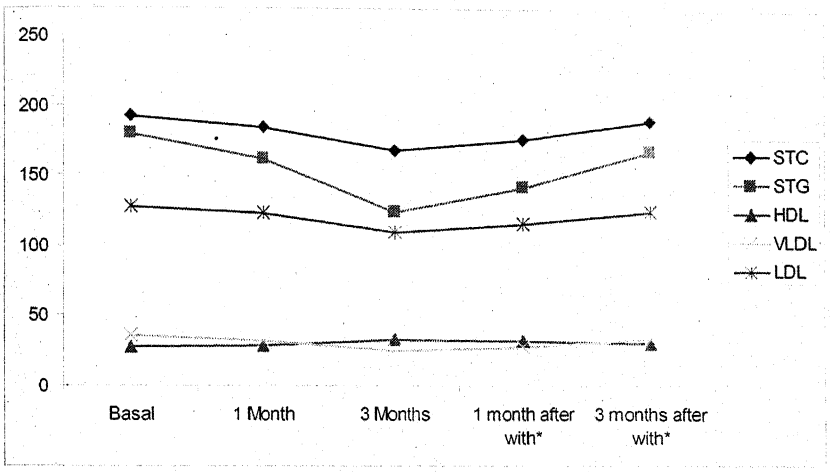
	In mg/dl					
	STC	STG	HDL	VLDL	LDL	LDL/HDL
Basal	240	278	32	56	152	4.8
1 Month	218	242	32	48	138	4.3
3 Months	190	204	34	41	115	3.4
1 month after with*	204	216	34	43	127	3.7
3 months after with*	236	254	33	51	152	4.6



NIACIN GROUP

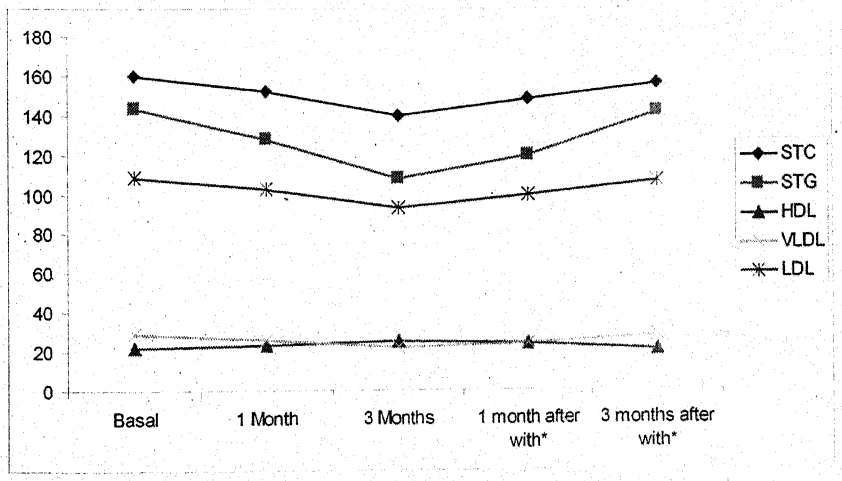
- **V.P. Agarwal**
- Age 52 Years/M
- Anterior wall MI

	In mg/dl					
	STC	STG	HDL	VLDL	LDL	LDL/HDL
Basal	192	180	28	36	128	4.6
1 Month	184	162	29	32	123	4.2
3 Months	168	124	33	25	110	3.3
1 month after with*	176	142	32	28	116	3.6
3 months after with*	190	168	31	34	125	4



- **Ghanshyam**
- Age 50 Years/M
- Systemic Hypertension

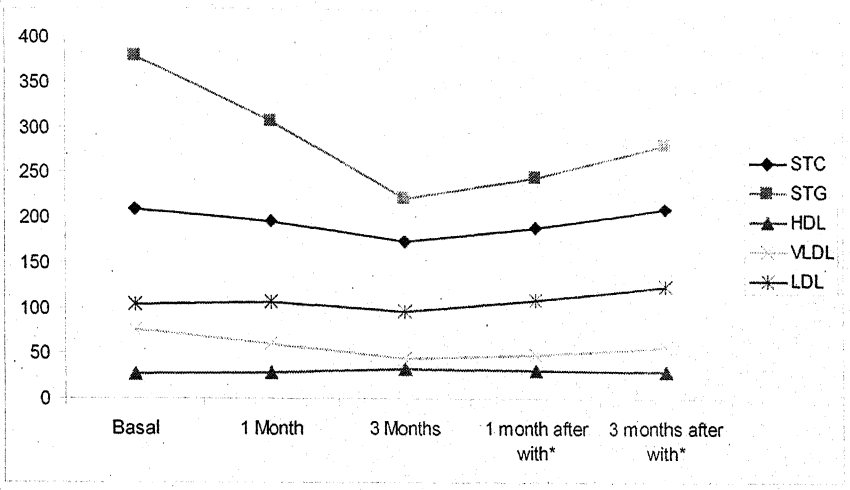
	In mg/dl					
	STC	STG	HDL	VLDL	LDL	LDL/HDL
Basal	160	144	22	29	109	5
1 Month	152	128	23	26	103	4.5
3 Months	140	108	25	22	93	3.7
1 month after with*	148	120	24	24	100	4.2
3 months after with*	156	142	21	28	107	5.1



NIACIN GROUP

- **Shiv Das**
- Age 45 Years/M
- CAD

	In mg/dl					
	STC	STG	HDL	VLDL	LDL	LDL/HDL
Basal	208	378	28	76	104	3.7
1 Month	196	306	29	61	106	3.7
3 Months	174	222	33	44	97	2.9
1 month after with*	190	246	32	49	109	3.4
3 months after with*	212	284	30	57	125	4.2



Discussion

This work was conducted in the Department of Medicine, ; M.L.B. Medical College, Jhansi on patients suffering from systemic hypertension. Diabetes Mellitus, Ischemic Heart Disease, Myocardial Infarction or Nephrotic syndrome

The Changes in Serum total cholesterol (STC) :

The values obtained were compared with the basal values.

Group - I (Atorvastatin Group) :

The mean basal fasting values of the patients in this group was 219.4 ± 27.49 while the values after 1 and 3 months of treatment and after 1 & 3 months of withdrawal are 200.25 ± 48.3, 190.17 ± 15.59, 196.96 ± 16.91, 208.63 ± 21.37 respectively.

Group – II (Fenofibrate Group) :

The mean basal fasting values of the patients in this group was 220.77 ± 38.16 while the values after 1 and 3 months of treatment and after 1 & 3 months of withdrawal are 203.62 ± 35.63, 181.69 ± 30.93, 191.77 ± 33.47, 213.54 ± 38.24 respectively

Group - III (Niacin Group)

The mean basal fasting values of STC of the patients in this group was 178.33 ± 35.69. The values after 1 and 3 months of treatment and after 1 & 3 month of withdrawal are 164.13 ± 36.26, 139.73 ± 29.39, 153.6 ± 28.41, 176.67 ± 31.33 respectively.

On statistical analysis we found that the serum cholesterol lowering effect of Atorvastatin Fenofibrate & Niacin were statistically very significant ($P<0.01$ in all groups) After 1 month of withdrawal cholesterol

lowering effect in all the three groups was very significant but after 3 months of withdrawal cholesterol lowering effects in Atorvastatin group was very significant (<0.01) but in Fenofibrate & Niacin group it is not significant.

The Changes in Serum triglyceride (STG) :

Group – *I (Atorvastatin* Group) :

The mean basal fasting values of STG of patients in this group was 118.96 ± 44.53. The values after 1 and 3 months of treatment and after 1 & 3 months of withdrawal are 111.5 ± 40.57, 104.29 ± 39.45, 108.54 ± 38.87, 114.33 ± 39.14 respectively.

Group - II (Fenofibrate Group)

The mean basal fasting value of STG of patients in this group was 375.31 ± 92.18, while the values after 1 and 3 months of treatment and after 1 & 3 months of withdrawal are 296.23 ± 82.52, 214.92 ± 63.33, 245.69 ± 71.85, 295.85 ± 71.63, respectively.

Group - III (Niacin Group) :

The mean basal fasting values of STG of patients in this group 206.27 ± 68.03, was while the value after 1 and 3 months of treatment and after 1 & 3 months of withdrawal are 177.93 ± 53.68, 135.27 ± 39.68, 156.2 ± 42.86, 189.8 ± 54.49, respectively.

On statistical analysis lowering of STG by Atorvastatin (P<0.01) Fenofibrate (P<0.01) and of Niacin (P<0.01) after 3 months of treatment was very significant. After 1 month of withdrawal lowering effect of Atorvastatin, Fenofibrate & Niacin was very significant. While after 3 months of withdrawal lowering effect of Atorvastatin was significant (<0.05), effect of Fenofibrate was very significant (<0.01) & effect of Niacin was not significant (>0.05).

The Changes in High density lipoprotein (HDL) :

Group – I (Atorvastatin Group) :

The mean basal fasting value of HDL in this group was 40.75 ± 3.37 while the values after 1 and 3 months of treatment and after 1 and 3 months of withdrawal are 39.96 ± 3.63, 39.91 ± 3.35, 39.58 ± 3.20, 38.42 ± 3.16 respectively.

Group - II (Fenofibrate Group) :

The mean basal fasting value of subjects in this group was 30.46 ± 9.21 while after 1 and 3 months of treatment and 1 & 3 months of withdrawal are 32.38 ± 8.46, 35.77 ± 8.49, 34.92 ± 8.32, 32.92 ± 7.95 respectively.

Group - III (Niacin Group) :

The mean basal fasting value of HDL of subjects in this group was 27.4 ± 4.29, while after 1 and 3 months of treatment and after 1 & 3 months of withdrawal are 27.8 ± 3.97, 30.13 ± 4.2, 29.47 ± 3.98, 27.73 ± 4.69 respectively.

On analysis changes in HDL are statistically insignificant after treatment in Atorvastatin group, but after 1 & 3 months of withdrawal decrease in HDL was significant, changes in HDL was statistically very significant in Fenofibrate group. After 3 months of treatment by Niacin changes in HDL was significant & after 1 month of withdrawal changes was significant but after 3 months of withdrawal changes are not significant.

The Changes in Very Low Density Lipoprotein (VLDL) :

Group – I (Atorvastatin Group) :

The mean basal fasting value of VLDL in subjects of this group was 23.88 ± 8.85 while the values after 4 and 12 weeks of treatment and after

1 & 3 months of withdrawal are 22.42 ± 8.04, 20.96 ± 7.88, 21.75 ± 7.82, 23 ± 7.79 respectively.

Group - II (Fenofibrate Group) :

The mean basal fasting values of the VLDL in subjects of this group was 75.23 ± 18.51, while the values after 1 and 3 months of treatment and after 1 & 3 months of withdrawal are 59.08 ± 16.46, 43 ± 12.58, 49.15 ± 14.5, 59.17 ± 14.96 respectively.

Group - III (Niacin Group):

The mean basal fasting values of the VLDL in subjects of this group was 41.25 ± 13.97, while the values after 1 and 3 months weeks of treatment and after 1 & 3 months of withdrawal are 35.59 ± 10.56, 27.05 ± 7.7, 31.24 ± 9.41, 37.96 ± 10.86 respectively.

On analysis the changes in VLDL in Atorvastatin group after 1 and 3 months of treatment was very significant. After 1 month of withdrawal changes are very significant but after 3 months of withdrawal changes are not significant.

In Fenofibrate group changes in VLDL during treatment and after withdrawal are very significant (<0.01).

In Niacin group changes are very significant (<0.01) after 1 & 3 months of treatment & after 1 month of withdrawal, but after 3 months of withdrawal changes are not significant.

The Changes in LDL (Low Density Lipoprotein) :

Group - *I* (Atorvastatin Group) :

The mean basal fasting value of LDL in subjects of this group was 147.29 ± 52.95, while the values after 1 and 3 months of treatment and

after 1 & 3 months of withdrawal are 142.04 ± 21, 129.38 ± 14.71, 136 ± 15.38, 147.29 ± 18.10 respectively.

Group - II (Fenofibrate Group) :

The mean fasting value of LDL in this group was 114.23 ± 31.42, while after 1 and 3 months of treatment and after 1 & 3 months of withdrawal are 112.38 ± 32.04, 102.92 ± 30.95, 107 ± 31.17, 120.08 ± 31.96, respectively.

Group - III (Niacin Group) :

The mean basal fasting value of LDL of subjects in this group was 110 ± 31.15, while after 1 and 3 months of treatment and after 1 & 3 months of withdrawal are 100.8 ± 32.11, 82.6 ± 24.06, 93 ± 24.79, 111.07 ± 26.41, respectively.

On statistical analysis the changes in LDL i.e. the lowering effect of LDL in the Atorvastatin groups were statistically very significant, 1 and 3 months of treatment. Values remain very significant after 1 & 3 months of withdrawal.

In Fenofibrate group changes in LDL was statistically insignificant after 1 & 3 months of treatment, values remain insignificant after 1 & 3 months of withdrawal.

In Niacin group changes in LDL was statistically very significant after 1 & 3 month of treatment, values remain significant after 1 month of withdrawal by it was not significant after 3 months of withdrawal.

The present study shows that Atorvastatin significantly reduces the total cholesterol & LDL cholesterol. Serum Triglyceride, but increase in HDL was not significant.

In a study pontrelli L Parris W Adelik Cheurg RC et al found that treatment by atorvastatin resulted in a statistically significant reduction in total cholesterol, LDL cholesterol, triglycerides and apoB. which are similar to our study.

In other study Atalar E. Ozmen F. Hazenedraoglu. I. Ault Ozer N. Ovuric K. Akroyek S. Kes. et al studied the effect of atorvastatin in hyperlipidemic patient with coronary artery disease and found that after treatment LDL, total cholesterol, triglyceride reduce significantly and HDL-c increases significantly. These results are similar to our study except in HDL-c which is not significantly raised in our study.

In our study Fenofibrate has significant effect on total cholesterol, S. triglyceride and HDL-c levels but effect on LDL-C is not significant.

In DAIS - Diabetes Atherosclerosis Intervention Study micronised fenofibrate was associated with significantly greater improvements from base line in STC, LDL-c HDL-c and TG levels, which differ from our study in LDL-c which is not significantly change in our study.

Badiou S. Merle De Boever S. Dupuy AM. Baillat V. Cristol JP. Reynes J. in 2004 Feb studied the effect of fenofibrate on lipid profile and found that after 3 months of treatment a significant decrease in STG, STC, non HDL-C and increase in HDL-c and apo A level, except LDL change, all results are similar to our study.

In our study we found that Niacin affect all modalites of lipid profile significantly after 3 months of treatment and after one month of drug withdrawal changes are not significant after 3 months of withdrawal.

Pan J. Van JT. Chan E. Kesala R.L. Lin M, Charles MA in 2002 sep studied the effect of Niacin on atherogenic lipid profile in diabetes and found that LDL cholesterol concentration reduce significantly, total HDL increased significantly and Lp_a level was improved significantly. These results match to our study results.

Mckenney JM, Mc Cormick LS. Schaefer EJ. Black DM, Watkins ML in 2001 Aug. studied effect of Niacin and atorvastatin on lipoprotein sub classes in patient with atherogenic dyslipidemia and found the similar results.

Summary and Conclusion

Summary and Conclusion

This study consisted of 52 subjects which were grouped into three groups, groups comprised of 24,13,15 subjects respectively. Individuals who were having ↑ LDL levels are in group I receiving atorvastatin 20mg/day. Individuals who were having ↑ triglyceride level (>250mg/dl) were in group II receiving fenofibrate 160mg/day and individual who were having ↓ HDL (< 35mg/dl) are in group III receiving niacin 500mg twice daily.

Atorvastatin significantly reduces total cholesterol serum triglyceride and LDL level after 3 months of treatment but HDL was not significantly raised. After 3 months of withdrawal, effect of treatment was significant on STC, STG & LDL levels.

Fenofibrate significantly reduces STC, STG & significantly increases S.HDL levels after treatment for 3 months, but LDL levels are not significantly reduced. After 3 months of withdrawal, effect of treatment was significant on STG, SHDL but was insignificant on STC & LDL.

Niacin significantly reduces STC, STG, LDL levels & raises SHDL levels after 3 months of treatment. After 1 month withdrawal effect of treatment was significant in all modalities, but after 3 months of withdrawal of treatment effect was not significant in all modalities.

Bibliography

Bibliography

- Atalar E, Ozmen F, Haznedaroglu 1, Acil T. OZer N. Ovunc K, AksoyeKS, Kes S. International Journal of cardiology 84(2-3) : 227-31 2002, Aug.

- Am.j Cordial 2001: 88(Suppl) : 30M-36M.

- Aguilar-Salinas, C.A.. Barrett. H., and Schonfed. G. Metabolic modes of action of the statins in the hyperlipoproteinemias. Atherosclerosis. 1998, 141:203-207.

- Albert. A.W., Chen. J., Kuron. G., Hunt, V., Huff, J., Hoffman. C., Rothrock, J., Lopez. M., Joshua, H., Harris. E., Patchett, A., Monaghan, R., Currie. S., Stapley, E., Albers-Schonberg, G., Hensens, O., Hirshrield. J., Hooasteen, K., Liesch, J., and Springer, J, Mevinolin: a highly potent, competitive inhibitor of hydroxymethyl-glutaryl-coenzyme A reductase and a cholesterol-lowering agent. *Proc. Natl. Acad. Sci. U.S.A.*, 1980, 77:3957-3961.

- Altschul, R., Hoffer, A., and Stephen J.D. Influence of nicotinic acid on serum cholesterol in man. Arch. Biochem. Biophys., 1955, 54:558-559.

- Arad, Y., Ramakrishnan, R., and Ginsberg, H.N. Lovastatin therapy reduces low density lipoprotein apo B levels in subjects with combined hyperlipidemia by reducing the production of apoB-containing lipoproteins : implications for the pathophysiology of apoB production. *J. Lipid Res., 1990, 31:567-582.*

- Athyros VG. Mikhailidis DP, Papageorgiou AA, Merouris BP, Athyrou VV, Symeonidis AN, Basayannis EO, Demitriadis DS,

Kantoponlon AG Atherosclerosis unit, Aritotelian university Hippocrotion Hospital , 49 Kanstantinoupolios St, Thenalini ki ,546-7, Greece.

- Albrink MJ, Man EB : Serum triglcerides in coronary artery disease. Arch Intern Med 4: 103, 1959-

- Barritt BW : Alimentary lipaemia in men with coronary artery disease and in controls. BMJ 2 : 640, 1956.

- Bouchier JAO, Bronte SB : Alimentary lipemia and ischaemic heart disease. Lancet 363 : 7173, 1961.

- Briones ER, Mao SJT, et al : Analysis of plasma lipids and apolipoproteins in insulin dependant and non-insulin dependant diabetes mellitus. Metabolism 33 : 42-49 ,1984.

- Bellosta S., Via, D., Canavesi, M., Pfister, P., Fumagalli, R., Paoletti, R., and Bernini, F, HMG-CoA reductase inhibitors reduce MMP-9 secretion by macrophages. Arterioscler, Thromb, Vasc. Biol., 1998, 18:1671-1678.

- Bilheimer, D.W., Grundy, S.M. Brown, M.S., and Goldstein, J.L. Mevinolin and colestipol stimulate receptor-mediated clearance of low density lipoprotein from plasma in familial hypercholesterolemia heterozygotes, *Proc. Natl Acad. Sci. U.S.A., 1983, 80:4124-4128.*

- Blum, C.B., Levy, R.I., Eisenberg, S., Hall III, Goebel, R.H., and Berman, M. High density lipoprotein metabolism in man. *J. Clin Invest., 1977, 60:795-807.*

- Brown, M.S., Faust, J.R., and Goldstein, J.L. Induction of 3-hydroty – 3-methylglutaryl coenzyme A reductase activity in human

fibroblasts incubated with compactin (ML-236B), a competitive inhibitor of the reductase, *J Biol, Chem., 1978, 253:1121-1128.*

- Berk- Planken II, Hoogerbrugge N, Stolk RP, Bootsma AH. Jamentti DALI study group/ Diabetes care 2003 Feb: 26 (2) : 427-32

- Bustos, C., Hernandez-Presa. M.A., Ortego, M., Tunin, J., Ortega. L., Perez, F., Diaz, C., Hermandez, G., and Egido, J, HMG-CoA reductase inhibition by atherosclerosis. *J. Am. Coll. Cordiol., 1998, 32:2057-2064.*

- Carlson LA, Bottiger LE : IHD in relation to fasting value of triglyceride and cholesterol. Stockholm prospective study. Lancet 1 : 865, 1972.

- Carlson, L.A. Hamsten , A. and Asplund, A. Pronounced lowering of serum levels of lipoprotein LP(a) in hyperlipidaemic subjects treated with nicotinic acid . I. Intern , Med. 1989,226: 271-276.

- Elam MB. Hunninghak DB. Darin KB. Gary R. Johnson C. Egan D, Kostis JB, Sheps DS, Brinten EA, JAMA, 284(10) : 1263-70, 2000 Sep 13.

- Grundy, S.M. Benjamin, I.J. Burke, G.L. Chait, A., Eckel ,R.H., Howard, B.V. Mitch ,W. Smith, S.C. Jr. and sawors, J.R. Diabetes and cardiovascular disease, a statement for health care professionals from the American heart association , circulation 1999 , 100: 1134-146.

- Grundy, S.M. Balady; G.J. Criqui, M.H. Fleteher, G. Greanland , P. Hiratzka, L.F., Hausten. Miller, N. Kris- Etherton , P. primary prevention of coronary heart disease. Guidance from Framingham : a statement for healthcare Proffersionals from the AHA. Task force,

an risk reduction American heart association. Circulation 1998, 97: 1876-1887.

- Grundy SM. Vega GL. Me Cavern ME. Tulloch BR. Kendall DM. Fitz- Patrick D. Ganda OP. Rosenson RS. Buso JB. Robertson DD. Steehan JP. Diabetes Multi center Research Group. Archive of Internal Medicine. 162(14): 1568- 76, 2002 Jul 22.

- Grundy, S.M., Mok, H.Y.I. Zech, L., and Berman, M. Influence of nicotinic acid on metabolism of cholesterol and triglycerides in man. *J. Lipid Res., 1981, 22:24-36.*

- Grundy, S.M.. and Vega, G.L. Influence of mevinolin on metabolism of low density lipoproteins in primary moderate hypercholesterolemia. *J. Lipid Res.,* 1985, 26:1464 -1475.

- Grundy, S.M., and Vega, G.L. Fibric acids: effects on lipids and lipoprotein metabolism. *Am. J. Med.*, 1987, &5-3-20.

- Gutstein, D.E., and Fuster. V. Pathophysiology and clinical significance of atheroselerotic plaque rupture. *Cardiwise. Res..* 1999,41:323-333.

- G.R., Burrows E., Retzlaff. B., and Poole. M. Contrasting effects of unmodified and time-release forms of niacin on lipoproteins in hyperlipidemic subjects: clues to mechanism of action of niacin. *Mesabolim* 1985, 34:642-650.

- Gofman JW, Detalla 0, Glaxier F, et al; The serum lipoprotein transport system in health, metabolic disorders, atherosclerosis and CHD. Plasma 2:413,1954.

- Hulley SB, Rosenman RH, Bowel RD, et al; Epidemiology as a guide to clinical decisions. An association between triglyceride and coronary artery disease. N Eng J Med 302 : 1383, 1980.

- Hussein. O., Rosenblat, M., Schlezinger. S., Keidar. S., and Aviram, M. Reduced platelet aggregation after fluvastatin therapy is associated with altered platelet lipid composition and drug binding to the platelets *Br. J. Clin. Pharmacol.*, 1997a, -44:77-84.

- Illingworth, D.R., Fibric acid derivative. In Drug treatment of Hyperlipidemia. Marcel Dekker New York , 1991,pp 103-138.

- Jin, F.Y., Kamanna, V.S., and Kashyap. M.L. Niacin accelerates in tracellular apoB degradation by inhibiting triacylglycerol synthesis in human hepatoblastoma (HepG2) cells. *Arterioscler. Thromb. Vasc. in Biol.*. 1999, 19:1051-1059.

- Kuo P.T. Dyslipidemia & coronary artery disease (104 reference) clinical cardiology 17(10:519-27,1999-86.

- Knopp, R.H. clinical profiles of plain versus sustained release niacin (Niaspan) and the physiologic rationale for nighttime dosing . Am J. Cardiol. 1998,82:240-280.

- Kersten, S. Desvergne, B. and Wahli, W. Roles of PPARs in health and disease. Nature , 2000 405:421-424.

- Keating GM, Ormrod D. Adis International Limited, Auckland, Newzealend . Drugs 2002: 62(13): 1909-44.

- Kannel WB : Contributions of the Framingham Study to the conquest of artery disease. Am J Cardiol 62 : 1109 -1112, 1988.

- Lewis B : Effect of diet and drugs : high density lipoprotein and atherosclerosis. Amsterdam Elvester / Worth Holland 1978 : 143.
- Loopes - Virella MF, Wohltmann HJ et al : Plasma lipids and lipoproteins in young insulin dependent diabetic patients in relation with control. Diabetologia, 21 : 216-23, 1978.
- LeRoux CW. Murphy E. Seed M et al , lipid clinic, charing cross Hospital , London .united Kingdom. Clin Ther 2002 Jul : 24(7) : 1154-60.
- Lacoste, L., Lam, J.Y.T., Hung, J., Letchacovski, G., Solymoss, C.B., and Waters, D, Hyperlipidemia and coronary disease. Correction of the increased thrombogenic potential with cholesterol reduction. *Circulation* 1995, 92:3172-3177.
- Laufs, U., La Fata. V., Plutzky, J., and Liao, J.K. Upregulation of endothelial nitric oxide synthase by HMG-CoA reductase circulation, 1998, 97:1129-1135.
- Martin. Jadraque ,R. Tato, F. Mortaza, J.M. Vega G.L. and Grundy S.M. Effectiveness of low dose crystalline nicotinic acid in men with low high density lipoprotein cholesterol levels . Arch. Intern. Med 1996, 156: 1081-1088.
- Multiple Risk Factor Intervention Trial Research Group : Multiple Risk Factor Intervention Trial : Risk factor changes and mortality results JAMA 248 :1465-1477,1982.
- Pantrelli L. Pan-is W. Acteli K. Cheuing R.C. Metabolism clinical and Experimental 51(3) : 334-42,2002 Mar.
- Parhofer KG. Laubach E. Barrett PH, J lipid et al 2003 Aprl.

- Pan J. Lin M. Kesala RL. Van J. Cherles MA Diabetes Research center , Tuitin , CA, USA Diabetes obes Metab 2002 Jul: 4(4) : 255-61.

- Rindare JP , Achacosa S,. Veteruns Affuim Medical center , Prescott, AZ, USA, Am J ther 1996 Sep : 3(9) : 637-639

- Staels ,B. and Auwera, J. Regulation ofapo A-l gene expression by fibrates. Atherosclerosis 1998, 137:519-523.

- Sposito AC. Santos RD. Amancio RF. Ramires JA John chapman M. Maranhao RC. Heart institute. university of Saopaulo Medical school, Sao Paulo Brazil Atherosclerosis 2003 Feb; 166(2) : 311-21.

- Sacks, P.M., Proffer, M.A., Moye, L.A., Rouleau. J.I., Rutherford. J.D., Cole, T.G., Brown, L., Warnica, J.W., Arnold, J,M,O., Wun, C.-C., Davis, B.R.- and Braunwald, E. The effect of pravastatin on coronary events after myocardial infarction in patients with average cholesterol levels. Cholesterol and Recurrent Events Trial investigators, N. Engl. J. Med., 1996. 335:1001-1009.

- Scandinavian Simvastatin Survival Study Group. Randomised trial of cholesterol lowering in 4444 patients with coronary heart disease: the Scandinavian Simvastatin Survival Study (4S). *Lancet 1994, 344:*1383-1389.

- Shepherd, J., Cobbe. S.M., Ford, I., Isles C.G., Lorimer. A.R., Mac Farlane, P.W., McKillop, J.H., and Packard C.J, Prevention of coronary heart disease with pravastatin in men with hypercholesterolemia. West of Scotland Coronary Preventior- Study Group. A'. *Engl. J. Veil.,* 1995. 333:1301-1307.

- Stein, E.A., Lane., M., and Laskarzewski, P. Comparison of statins in hypertriglyceridemia. *Am. J. Cardiol.*, 1998, 81:66B-69B.

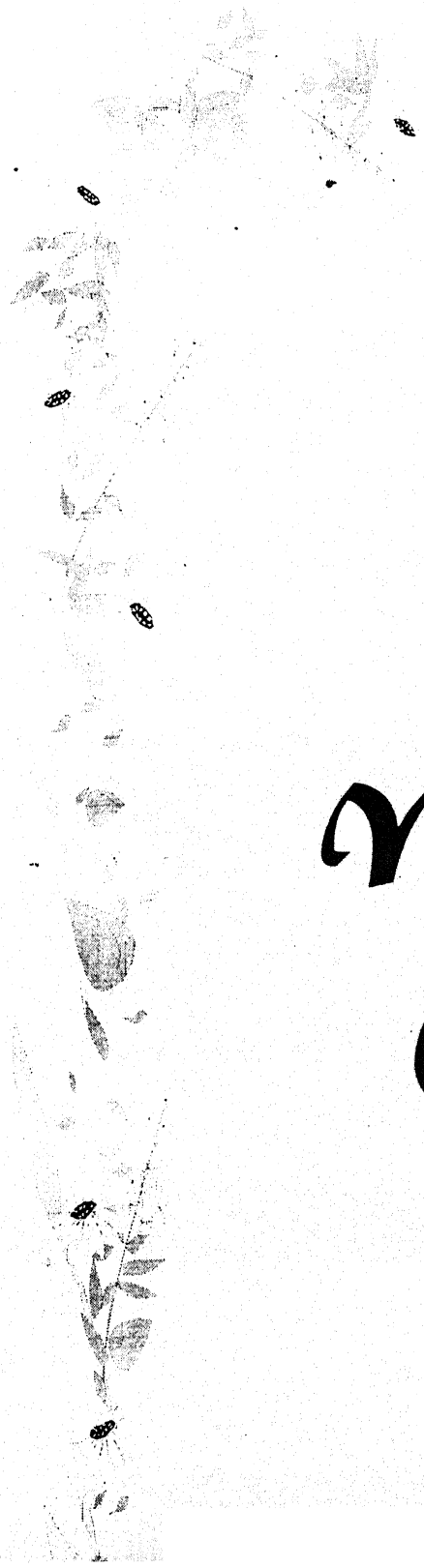
- Stamler, J. Wentwerth, D. and Neaten, J.D. In relationship between S. cholesterol and risk of premature death from coronary heart disease continuous and graded? Findings in 356,222 primary screenings of the multiple risk factor Intervention Trial [MRFIT], JAMA, 1986,256:2823-2828.

- Thompson, G.B. and Barter, P.J. clinical lipidology at the end of the millennium. Curr. Opin. Lipidol 1999,10:521-526

- Vega. G.L., and; Grundy. S.M. Lipoprotein responses to treatment with lovastatin, gemfibrozil and nicotinic acid in normolipidemic patients with hypoalphalipopropeinemia

- Watts. G.F. and Dimmitt,S.B. fibrates, dyslipoproteinaemia and cardiovascular disease. curropin . Lip idol, 1999, 10: 561-574.

- Welsan, P.W.F,, D. Agostino, R.B. Levy D. Belanger , A.M. Sclhershatzi H. and Kannel , W.B. Prediction of coronary heart disease using risk factor categories, circulation 1998,97:1837-1847.



Master Chart

MASTER CHART

GROUP - I ATORVASTATIN

S.N.	Name	Basal					1 Month					3 Month					1 Month after withdrawl					3 Month after withdrawal				
		STC	STG	HDL	VLDL	LDL	STC	STG	HDL	VLDL	LDL	STC	STG	HDL	VLDL	LDL	STC	STG	HDL	VLDL	LDL	STC	STG	HDL	VLDL	LDL
1	Ramesh	280	300	38	60	182	224	280	38	56	130	208	274	39	55	114	224	274	39	55	130	260	280	39	56	165
2	Hari Prasad	200	144	40	29	131	180	138	42	28	108	172	133	42	27	103	183	133	45	27	110	186	140	45	28	113
3	Arjun Pal Singh	216	136	48	27	141	190	134	49	27	114	190	126	49	25	116	194	128	47	26	121	197	130	47	26	124
4	Beni Bai	208	100	42	20	146	198	100	35	20	143	185	90	40	18	127	192	94	40	19	133	200	98	40	20	140
5	Shankar Lal	260	148	45	30	185	266	141	46	28	192	202	94	41	19	142	212	100	40	20	152	236	112	38	22	176
6	Indra Dev	200	95	40	19	141	192	88	40	18	134	184	88	41	18	125	186	90	40	18	128	192	98	40	20	132
7	Raja Ram	200	106	40	21	139	194	100	41	20	133	186	90	40	18	128	190	94	40	19	131	200	98	38	20	142
8	Nathu Ram	199	88	38	18	143	190	86	38	17	135	184	90	40	19	125	186	90	41	19	126	196	98	39	20	137
9	Rustam Khan	190	90	36	18	136	185	88	34	18	133	174	86	38	17	119	178	88	38	18	122	186	94	36	19	131
10	Mewa Ram	200	96	38	19	143	194	90	35	18	141	188	88	35	18	135	192	92	33	18	141	198	96	34	19	145
11	Ram Khilawan	228	110	43	22	163	206	100	41	22	145	200	100	38	20	142	210	106	38	21	151	214	108	37	22	155
12	Kiran Singh	280	160	45	32	203	260	146	44	29	187	224	132	47	26	151	236	140	45	28	163	250	148	43	30	177
13	Bhagwan Das	240	132	42	26	172	228	121	44	24	160	204	110	40	22	142	214	116	40	23	151	230	124	38	25	167
14	Vimla Saxena	215	100	41	20	154	200	92	40	18	142	192	90	40	18	135	196	92	40	18	138	204	96	38	19	147
15	Bilasi Ram	198	100	40	20	138	190	98	40	20	130	180	90	40	18	122	186	94	39	19	128	192	96	39	19	136
16	Shiv Darsan	228	140	44	28	156	191	94	40	19	132	160	110	38	22	100	174	126	40	25	109	200	132	38	26	136
17	N.P. Junar	237	90	35	19	184	230	90	36	19	176	210	90	35	19	157	218	94	35	19	164	232	98	36	20	179
18	Yashwant Nagar	215	110	42	22	151	195	90	40	18	137	188	86	41	17	130	192	92	40	18	144	214	100	38	20	156
19	Laxman Singh	188	89	35	19	135	180	90	36	19	126	175	70	36	14	125	182	76	35	15	132	190	80	34	16	140
20	Sharda	210	90	40	18	152	191	100	40	20	131	170	80	40	16	114	180	90	39	18	123	188	94	38	19	31
21	Shiv Ram Singh	200	96	40	19	141	190	94	40	19	131	186	90	38	18	130	188	90	38	18	132	196	98	36	20	140
22	Sooraj	210	100	38	20	152	200	100	36	20	144	196	95	36	19	141	198	98	36	20	142	206	104	36	21	49
23	Gayatri	200	95	42	19	139	192	90	41	18	133	186	90	41	18	127	188	92	40	18	130	198	98	38	20	140
24	N.C. Jain	264	140	46	28	190	240	126	43	25	172	220	111	43	22	155	228	116	42	23	163	242	124	40	25	177

MASTER CHART

GROUP - II FENOFIBRATE

S.N.	Name	Basal					1 Month					3 Month					1 Month after withdrawl					3 Month after withdrawal				
		STC	STG	HDL	VLDL	LDL	STC	STG	HDL	VLDL	LDL	STC	STG	HDL	VLDL	LDL	STC	STG	HDL	VLDL	LDL	STC	STG	HDL	VLDL	LDL
1	Radha Rani	212	506	12	101	114	202	346	13	69	120	187	190	17	38	132	192	198	17	40	135	198	240	15	48	135
2	Dr Adarsh Srivastava	232	513	23	103	106	183	466	29	93	60	166	324	30	65	71	174	380	28	76	71	192	404	26	81	85
3	R.K. Ojha	166	394	23	79	64	162	203	30	41	91	154	158	34	32	88	158	176	34	35	89	166	208	33	42	75
4	K.C. Pandey	203	454	38	91	74	192	407	39	81	72	180	322	41	64	75	191	354	41	71	69	212	380	39	76	97
5	Mohd Jalal	238	281	50	56	106	191	227	50	45	96	154	188	56	38	60	168	196	54	39	75	216	242	50	48	118
6	M.S. Khan	231	323	36	65	130	208	286	36	57	115	167	160	35	32	100	190	204	36	41	113	224	268	35	54	135
7	Shiv Khare	248	296	34	59	155	231	242	35	48	148	186	172	38	34	114	196	192	38	38	120	242	264	36	53	153
8	Rambitar	286	418	36	84	166	270	348	38	70	162	242	274	40	55	147	254	308	39	62	153	292	388	37	78	177
9	Laltu Prasad	192	266	26	53	113	184	212	28	42	114	172	154	33	31	108	178	180	31	36	111	188	224	30	45	113
10	Veer Singh	286	478	33	96	157	274	342	34	68	172	260	286	37	57	166	268	314	36	63	169	280	384	34	77	169
11	Prabha Devi	196	278	26	56	114	184	232	27	46	111	162	186	33	37	92	176	212	32	42	102	188	246	30	49	109
12	Uma Shankar	168	288	28	58	82	160	224	30	45	85	148	168	35	34	79	156	196	33	39	84	172	258	30	52	90
13	Ram Achal	212	384	31	77	104	206	316	32	63	111	184	212	36	42	106	192	284	35	57	100	206	340	33	68	105

MASTER CHART

GROUP - III NIACIN

S.N.	Name	Basal					1 Month					3 Month					1 Month after withdrawl					3 Month after withdrawal				
		STC	STG	HDL	VLDL	LDL	STC	STG	HDL	VLDL	LDL	STC	STG	HDL	VLDL	LDL	STC	STG	HDL	VLDL	LDL	STC	STG	HDL	VLDL	LDL
1	Rameshwar	138	232	26	46	66	100	180	27	36	37	84	111	28	22	34	112	200	26	40	46	151	281	23	56	72
2	Hari Babu Sharma	131	130	25	26	80	120	96	26	19	75	104	72	28	14	62	116	90	28	18	70	138	118	27	24	87
3	Ramesh Chand Gupta	141	139	32	28	81	128	121	33	24	71	114	108	36	22	56	122	114	37	23	62	136	120	35	24	77
4	Om Prakash	173	163	34	33	106	160	152	34	30	96	146	138	37	28	81	158	148	36	30	92	175	160	35	32	108
5	Yashwant Singh	132	154	25	31	76	126	148	26	30	70	110	100	28	20	62	124	116	27	23	74	140	138	24	24	92
6	P.V. Sharma	186	258	24	52	110	174	208	25	42	107	140	152	27	30	83	154	172	26	34	94	184	200	25	40	119
7	Dinesh	212	162	30	32	150	200	154	30	30	140	154	116	32	23	99	160	130	31	26	103	186	170	29	34	123
8	Moti Ram	194	264	28	53	113	182	224	29	45	108	130	146	31	29	70	148	172	30	34	84	178	228	28	46	104
9	Shireen	224	180	29	36	159	210	166	30	33	147	174	120	31	24	119	190	138	31	28	131	224	188	29	38	157
10	Avtar Singh	200	192	18	38	144	180	164	19	33	128	140	136	22	27	91	166	148	21	30	115	192	168	20	34	138
11	Kamal	144	240	24	48	72	132	218	25	44	63	128	172	27	34	67	136	191	26	38	72	152	228	26	46	80
12	K.K. Kulshrestra	240	278	32	56	152	218	242	32	48	138	190	204	34	41	115	204	216	34	43	127	236	254	33	51	152
13	V.P. Agarwal	192	180	28	36	128	184	162	29	32	123	168	124	33	25	110	176	142	32	28	116	190	168	31	34	125
14	Ghanshyam	160	144	22	29	109	152	128	23	26	103	140	108	25	22	93	148	120	24	24	100	156	142	21	28	107
15	Shiv Das	208	378	28	76	104	196	306	29	61	106	174	222	33	44	97	190	246	32	49	109	212	284	30	57	125